Modelling the impact on Hepatitis C transmission of reducing syringe sharing: London case study

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Background Hepatitis C virus (HCV) prevalence and incidence among injecting drug users (IDUs) has increased in London and rest of UK. To inform public health action, mathematical modelling is used to explore the possible impact of strategies to decrease syringe sharing.

Methods A mathematical model was developed to simulate HCV transmission amongst IDUs in London. Because of parameter uncertainty, numerical search algorithms were used to obtain different model fits to HCV seroprevalence data from London for 2002–03. These simulations were used to explore the likely impact of HCV prevention activities that reduce syringe sharing amongst all IDUs, IDUs that have injected for greater than one year, or IDUs with lower or higher frequencies of syringe sharing.

Results Key differences between model fits centred on how they simulated the high HCV incidence amongst new injectors, either through assuming increased HCV infectivity during acute infection, a large sub-group of high frequency syringe sharers, or increased sharing among new IDUs. Despite parameter uncertainty, the model projections suggest that modest reductions in syringe sharing frequency (<25%) will reduce the HCV seroprevalence in newly initiated IDUs (injecting less than four years) but much larger and sustained reductions (>50%) are required to reduce the HCV seroprevalence in long-term IDUs (injecting more than 8 years). Critically the model also suggested that large reductions in HCV seroprevalence will be achieved only if interventions target all IDUs and reach IDUs within 12 months of injecting.

Discussion Public health interventions must reduce syringe sharing amongst all IDUs, including newly initiated IDUs, and be sustained for many years to reduce HCV infection. More accurate data on key behavioural (sharing frequency) and biological (percentage of infected IDUs that clear infection) parameters is required to improve model projections.

Keywords Hepatitis C, modelling, injecting drug use, UK

Introduction World wide, 170 million people are estimated to be infected with Hepatitis C (HCV) virus, while 9 million are thought to be infected in Europe.1,2 HCV can be easily transmitted through blood products and infected syringes,3–6 and infection rates are typically high amongst IDUs.7–9 HCV infection is an important public health concern because the majority of infections do not resolve but lead to chronic infection.10–17 After 30 years, approximately 30% of the people chronically

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infected with HCV develop cirrhosis of the liver and once cirrhosis has developed 1–4% of individuals per year progress to liver cancer (hepatocellular carcinoma) which often leads to death.\(^{18}\)

In the UK, and other countries that have safe blood supplies and low iatrogenic risk, the prevention of HCV depends largely on reducing transmission among injecting drug users (IDUs). Indeed, the population burden of HCV is closely related to the number of people with an injecting history. In the UK, there are an estimated 200,000–500,000 people infected with HCV, over 90% of diagnoses are attributable to IDU,\(^{19}\) and over 40% of the current IDU population are HCV antibody-positive.\(^{19,20}\) The annual cost of treatment or care for individuals with chronic HCV infection are currently estimated to be €750 million for the European Union and €100 million for the UK.\(^{21}\) This highlights the importance of prevention interventions, especially considering the number of hepatocellular and carcinoma deaths that are projected to increase.\(^{22,23}\)

Syringe distribution and other interventions seeking to reduce syringe sharing are the main strategies for preventing the transmission of blood-borne viruses amongst IDUs.\(^{24}\) However, although syringe exchange interventions and the provision of methadone are associated with reduced HIV transmission,\(^{25–27}\) the evidence of their impact on HCV transmission is modest.\(^{28–31}\) Indeed, evidence suggests that current prevention strategies are insufficient in London and elsewhere in the UK because HCV and HIV transmission among IDUs are increasing.\(^{19,32–34}\)

Clearly, the size of the problem and the serious long-term consequences make HCV an important public health concern.\(^{35–37}\) In this analysis, we develop a mathematical model for simulating the transmission of HCV. The model is fitted to HCV antibody prevalence (sero-prevalence) data from London, UK, for 2002–03 in order to explore the nature of HCV transmission in this setting, and to determine the possible impact of prevention activities that reduce the frequency of syringe sharing amongst IDUs. The model is built on previous studies that have developed mathematical models of the epidemiology of HCV,\(^{38,39}\) or have estimated the impact of harm reduction interventions on HCV transmission,\(^{38,40}\) in order to inform policy-makers and public health action.

**Methods**

The analysis involved several steps. First, a HCV model was developed based on data available in the literature. Then, because of uncertainty in key biological and behavioural parameters, the model was fit in a staged process to HCV sero-prevalence data from London (2002–03). The different model fits were then used as a baseline comparison that could be used to estimate the potential impact of reductions in sharing behaviour on HCV transmission.

**Model structure**

The initial form of the model is an adaptation of a model developed by Kretzschmar and Wiessing,\(^{39}\) modified to allow for two types of acute infection, one leading to chronic infection and the other leading to resolved infection (allows for differences in viraemia during acute phase). Appendix I shows the flow diagram for the model.

The model simulates the transmission of HCV in a cohort of IDUs that start injecting at the same point in time. It assumes all new IDUs are susceptible and simulates the dynamics of infection over their duration of injecting ‘\(i\)’. Susceptible IDUs (\(x\)) are infected at a per capita rate ‘\(\pi\)’ through the use of infected syringes.\(^3\) Some epidemiological studies report an association between HCV infection and sharing of paraphernalia.\(^\text{1–6}\) However, this was not explicitly included in the model due to a lack of data on both the transmission probability and frequency of paraphernalia sharing. Sexual risk is assumed to be low.\(^{41–43}\) All newly infected IDUs become HCV RNA-positive (active infection) and progress to a phase of acute infection (duration 1/\(\sigma\) which lasts for 6–24 weeks,\(^{1,6,44–46}\) during which individuals usually develop an antibody response (anti-HCV-positive)\(^{11,13,15–17,44}\) and may have elevated viraemia,\(^{16,17,44}\) and so could be more infectious. Acute infections are divided into those that resolve their infection (proportion ‘\(\gamma\)’) after the acute phase (\(h2\))\(^{10,13,17}\) or progress to chronic infection (\(h1\)). Chronic infecteds (\(y\)) are assumed to remain infected (HCV RNA-positive) and anti-HCV-positive until death. IDUs that resolve their infection are assumed to become HCV RNA-negative, immune for life\(^{48–52}\) and are initially anti-HCV-positive (\(z1\)), but may lose their antibody response (seroconvert \(z2\)) after an average duration 1/\(\eta\).\(^{51,52–55}\)

The corresponding differential equations for the initial version of the model are as follows:

\[
\begin{align*}
\frac{dx}{da} &= -x((\pi + \mu) \\
\frac{dh1}{da} &= \pi_x(1-\delta) - h1(\sigma + \mu) \\
\frac{dh2}{da} &= \pi_x \delta - h2(\sigma + \mu) \\
\frac{dy}{da} &= \sigma h1 - \mu y \\
\frac{dz1}{da} &= \sigma h2 - z1(\mu + \eta) \\
\frac{dz2}{da} &= \eta z1 - \mu z2
\end{align*}
\]

The equation shows that in addition to stratifying IDUs by HCV infection status, they are also stratified into three levels of syringe sharing signified by the subscript ‘\(i\)’: none (\(i = 0\)), low frequency (\(i = 1\)) and high frequency (\(i = 2\)), although the overall average syringe sharing rate is kept constant across all syringe sharers. IDUs in the low- and high- frequency syringe-sharing groups mix with each other to form syringe-sharing partnerships. The degree of mixing between the sub-groups can vary from random to completely assortative. Due to a lack of detailed data on the cessation rate of IDUs in London, it is assumed that IDUs leave the population at a constant per capita rate ‘\(\mu\)’ due to death or cessation of injecting. Over small time-steps, the per capita rate of infection ‘\(\pi_i\)’ is the same as the average probability per unit time that a susceptible IDU in syringe-sharing group ‘\(i\)’ becomes infected with HCV, and is dependent on the number of IDUs in the acute and chronic phase of HCV infection, the probability of HCV transmission per syringe-sharing incident for each phase of infection, and the syringe-sharing behaviour of the IDU. The parameter ‘\(\pi_i\)’ is assumed to be zero for IDUs that do not syringe share (\(i = 0\)).
If an IDU has \( m_i \) syringe-sharing partners per unit time then \( \pi_i \) is the sum of the probabilities that the IDU will get infected from any of these partners. For each of these syringe-sharing partners, there is a certain probability that they will be a low or high syringe-sharer (\( \rho_{ij} \), where \( i \) and \( j \) denote the syringe-sharing sub-group of the IDU and their partner, respectively), which then determines the probability that their partner will be in the acute or chronic phase of infection, and the probability of being infected by this IDU per unit time (\( B_k \)). This gives the following formulation for \( \pi_i \) (for \( i = 1 \) or 2):

\[
\pi_i = \sum_{j=1 \ldots 2} m_i \rho_{ij} \left[ B_1 \frac{h_1}{N_j} + B_2 \frac{h_2}{N_j} + B_1 \frac{y_j}{N_j} \right],
\]

where \( B_k = (1 - (1 - \beta_k)^n) \), and \( n \) is the number of times that an IDU receptively shares syringes with each of their partners per unit time. \( \beta_k \) is the HCV transmission probability per syringe-sharing act (\( k = 1 \) if sharing with an IDU in the acute phase leading to chronic infection, \( k = 2 \) if sharing with an IDU in the acute phase of an infection that resolves, and \( k = 3 \) if sharing with an IDU in the chronic phase), and \( N_j \) is the number of IDUs that do not share (\( j = 0 \)), or syringe share with low (\( j = 1 \)) or high frequency (\( j = 2 \)). For a particular IDU (syringe-sharing sub-group \( i \)), the probability \( \rho_{ij} \) that a particular syringe-sharing partner is a low- (\( j = 1 \)) or high- (\( j = 2 \)) frequency syringe sharer is calculated using a standard method,\(^46\) by estimating the proportion of all syringe-sharing partners provided by that syringe-sharing sub-group and weighing it by a parameter \( \theta \) that denotes the degree of assortative mixing (\( \theta = 0 \) for random mixing and 1 for fully assortative):

\[
\rho_{ij} = \frac{N_i m_{ij}}{N_1 m_1 + N_2 m_2} (1 - \theta) + \theta b_{ij},
\]

here \( b_{ij} \) is the dirac-delta function, and equals one if \( i = j \) and zero otherwise. Lastly, the model allowed recently initiated ‘new’ injectors (IDUs injecting for less than one year) to have a higher frequency of syringe sharing (\( m_1 \) is scaled up by a factor \( \alpha \)) and to share partly with older injectors (with a greater HCV seroprevalence). This heterogeneity was incorporated as a possible reason for the high HCV incidence observed amongst ‘new’ IDUs in London, and because other studies have reported similar behaviours amongst recently initiated IDUs.\(^{57,58}\)

### Parameterizing the model

The model was parameterized using data from a number of sources, and these are shown in Table 1 with their uncertainty bounds. HCV serorelevance data (based on oral fluid tests which have over 90% sensitivity and 99% specificity for HCV antibody\(^{59}\)) against duration of injecting was obtained from a prospective cohort study and routine surveillance data from London for 2002–03.\(^{19,32,60}\) The cohort study recruited over 400 IDUs from community settings and networks; and routine surveillance data were available on over 1000 IDUs recruited from specialist drug treatment and syringe exchange agencies. All IDUs reported injecting in the last 4 weeks before recruitment, and completed an injecting risk questionnaire. These studies are the key source of data on HCV prevalence in London, and contribute to surveillance in the UK.

Unfortunately, no direct data were available on the frequency with which IDUs share, and so a proxy estimate was generated based on the estimated shortfall between the injection frequency, the number of syringes distributed and average syringe re-use.\(^{61,62}\) This estimate was used as the overall average syringe- sharing rate amongst all syringe sharers, and was kept constant in the fitting process. There was also no data on the number of people IDUs share with per month and so the \( B_k \) terms in equation (2) were expanded to obtain the product of \( n \) and \( m_i \) (the total syringe- sharing frequency in different syringe- sharing groups) in the formulation of \( \pi_i \). Data on other important aspects of IDU risk behaviour were also lacking, and so were given large uncertainty bounds, such as the degree of mixing between IDUs with different sharing rates (\( \theta \)); the proportion of IDUs with different sharing frequencies; the percentage of new IDUs that share with older IDUs; and the degree to which new IDUs share with a higher frequency than older IDUs (\( \alpha \)). The rate of leaving the population (\( \mu \)) was assumed to be 10% per year.\(^{63}\)

Estimates for the HCV biological parameters were obtained from the scientific literature. However, several biological parameters were uncertain, such as the proportion of infected IDUs that resolve their infection.\(^{10–17}\) In addition, the HCV transmission probability per needle-sharing act (1–10%) was estimated by multiplying the HIV transmission probability per IDU syringe-sharing act (0.63–2.4%)\(^{64,65}\) by the factor difference between the HCV transmission probability following needle-stick injury (0.31–9%)\(^{3,66}\) and the corresponding HIV needle-stick transmission probability (0.25%, 95% CI 0.01–0.49%).\(^{67}\) Because of the large degree of uncertainty in this parameter, any uncertainty in the frequency of syringe sharing was also assumed to be accounted for in this parameter.

### Methods for modelling the transmission of HCV in London

The model simulates the transmission of HCV against duration of injecting and was fitted to cross-sectional epidemiological data on HCV sero-prevalence from London for 2002–03.\(^{10,60}\) No single ‘best fitting’ model simulation could be determined because of the large degree of uncertainty present in the model parameters. Therefore, a numerical search algorithm was used to find different possible model fits from different starting points in the parameter uncertainty space.\(^{58}\) The model fitting process had a number of stages.

First, random sampling was used to obtain 1000 model parameter sets from the uncertainty ranges for each parameter.\(^{69}\) Second, using quarter monthly time steps the model was run with each parameter set, and the chi-squared error between each simulation and the epidemiological data was calculated and ranked.\(^{70}\) Third, the 20 best fitting parameter sets were used as starting points for using a numerical optimization algorithm (Newton’s method used in the Solver tool of Excel) to find local optima that minimize the chi-square error. Fourth, the process was replicated for 10 additional model parameter sets sampled randomly from the remaining 980 simulations of the uncertainty analysis, thus generating 30 best-fits of the
model to the cross-sectional HCV seroprevalence data. Fifth, the best-fits from this analysis were grouped together into classes with similar characteristics as defined by their parameter values. Finally, the model simulation with the smallest chi-squared error from each of these model types was selected for the following analyses.

**Impact of decreasing syringe sharing on transmission of HCV**

The model simulations were used to explore the likely impact of specific decreases in syringe sharing on HCV seroprevalence. The model was used to explore the effect of reduction in syringe-sharing amongst: all IDUs, IDUs injecting for greater than one year and IDUs with lower- or higher-frequencies of syringe-sharing.

**Results**

Figure 1 shows that the best-fit model simulation and the lower and upper bounds of the other 30 best-fits accurately project the observed HCV sero-prevalence in London for 2002–03. Critically, HCV sero-prevalence increases rapidly among recent IDUs with over 20% infected within 2 years of injecting.

Four classes of model type (A–D) were identified with the following common attributes: no change in the transmission probability during acute infection amongst those IDUs that resolve infection; a very low proportion (<4%) of new IDUs sharing with older IDUs; 60% or more of IDUs sharing syringes; IDUs mainly sharing syringes with IDUs with similar sharing rates; and IDU sub-groups with low- and high-frequencies of syringe sharing. The key differences between the model types was in how they simulated the high incidence of HCV infection observed amongst new injectors. One of the following combinations was required: a large sub-group of high-frequency syringe sharers either with a low (class C) or high proportion that resolve infection (class A); or a smaller sub-group of high-frequency syringe sharers and either new IDUs have a higher sharing rate (class B) or acute infected individuals have an increased HCV transmission probability before they progress to chronic infection (class D). Although they all closely fitted the observed data, projecting the same HCV sero-prevalence for IDUs injecting for less than eight years (≈44%), they give different projections for the proportion of IDUs that are actively infected (RNA-positive) or have resolved their infection (RNA-negative and immune), ranging from 25% to 35% and 7–25%, respectively. Table 2 shows the

<table>
<thead>
<tr>
<th>Table 1 Biological, behavioural and epidemiological parameter values for HCV model</th>
<th>Parameter notation</th>
<th>Parameter range</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV Biological parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmission probability per syringe-sharing act in chronic infection phase</td>
<td>$\beta$</td>
<td>0.84–10%</td>
<td>3,6,6,7,66</td>
</tr>
<tr>
<td>Ratio of initial peak of viraemia to viraemia in chronic phase</td>
<td>$\beta_{2}/\beta_{3}$</td>
<td>1–10</td>
<td>16,17,44</td>
</tr>
<tr>
<td>Ratio of initial viraemia peak to viraemia in chronic phase for those that resolve their infection</td>
<td>$\beta_{2}/\beta_{3}$</td>
<td>0.1–1</td>
<td>15–17</td>
</tr>
<tr>
<td>Duration of acute phase</td>
<td>$1/\alpha$</td>
<td>6–24 weeks</td>
<td>11–16,44–46,77</td>
</tr>
<tr>
<td>Proportion of infecteds that resolve their infection</td>
<td>$\delta$</td>
<td>18–50%</td>
<td>10–17</td>
</tr>
<tr>
<td>Duration till sero-convert after infection</td>
<td></td>
<td>2–14 weeks</td>
<td>44,77–80</td>
</tr>
<tr>
<td>Duration till lose antibody response after resolve infection</td>
<td>$1/\eta$</td>
<td>7–15 years for serum test. Less for oral tests.</td>
<td>17,51,53–55,77,81</td>
</tr>
<tr>
<td><strong>London HCV epidemiological parameters amongst IDUs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV seroprevalence</td>
<td></td>
<td>&gt;50%</td>
<td>19</td>
</tr>
<tr>
<td>HCV seroincidence</td>
<td></td>
<td>&gt;30%</td>
<td>32</td>
</tr>
<tr>
<td><strong>London IDU behavioural parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of IDUs reporting syringe sharing</td>
<td>$(N1 + N2)/(N0 + N1 + N2)$</td>
<td>33% in last month, 66% at least once</td>
<td>60</td>
</tr>
<tr>
<td>Average frequency of syringe injecting</td>
<td></td>
<td>700 per year</td>
<td>62</td>
</tr>
<tr>
<td>Number of syringes distributed to each IDU</td>
<td></td>
<td>140 per year</td>
<td>62</td>
</tr>
<tr>
<td>Mean frequency of syringe re-use before disposal</td>
<td></td>
<td>3.5 times</td>
<td>60</td>
</tr>
<tr>
<td>Estimated frequency of syringe sharing</td>
<td>$\bar{m}$</td>
<td>~16 per month</td>
<td>Estimated from data in 62</td>
</tr>
<tr>
<td>Percentage of IDUs in higher frequency syringe-sharing sub-group</td>
<td>$N2/(N1 + N2)$</td>
<td>0–50% of those that share</td>
<td>No data available</td>
</tr>
<tr>
<td>Factor increase in sharing rate amongst high-frequency syringe sharing IDUs</td>
<td>$m2/m1$</td>
<td>1–10</td>
<td>No data available</td>
</tr>
<tr>
<td>Percentage of IDUs at the start of their injecting career that share with older IDUs</td>
<td></td>
<td>0–100%</td>
<td>No data available</td>
</tr>
<tr>
<td>Factor increase in syringe sharing frequency amongst IDUs at the start of their injecting career</td>
<td>$\alpha$</td>
<td>1–10</td>
<td>No data available</td>
</tr>
</tbody>
</table>
precise differences in the parameter values and summary projections for the different model types.

For the following analyses, we have focused on the best-fits for class A, B and C, as D gave similar projections to A.

**Impact of decreasing syringe sharing in all IDUs**

Figure 2 shows the impact of decreasing syringe-sharing amongst all IDUs on HCV seroprevalence for models A and B (model C projections are similar to A). First, the figure shows that for model A, a modest decrease in syringe sharing will result in a notable decrease in HCV seroprevalence amongst IDUs that have been injecting for 1 year. In contrast, for model B, which assumes a small sub-group of higher frequency syringe sharers, a much greater decrease in syringe sharing is required to decrease the HCV seroprevalence. Amongst IDUs who have been injecting for 4 years, relatively modest decreases in syringe sharing result in reductions in HCV seroprevalence in both models. However, amongst IDUs that have been injecting for longer, more substantial decreases in syringe sharing, up to 25–50%, are required to achieve notable decreases in HCV sero-prevalence. For example, amongst IDUs that have been injecting for 8 years, syringe sharing has to decrease by at least 25%, from 16 to 12 receptive syringe-shares per month, for any decrease in HCV sero-prevalence to occur. Lastly, to reduce HCV seroprevalence to <10% amongst all IDUs that have been injecting for ≤8 years, the rate of syringe sharing has to decrease to about 1–2 times a month (see Figure 3 for these projections). Furthermore, any projected reductions in HCV seroprevalence assume that the reduction in syringe sharing is sustained over an IDU’s injecting life course, i.e. for at least 8 years for these projections.

**The importance of reaching all injectors**

Figure 3 compares the relative impact on HCV infection of reducing syringe sharing amongst all IDUs or only amongst IDUs who have been injecting for >1 year. The model projections suggest that HCV seroprevalence can be reduced even with moderate reductions in sharing. However, as syringe sharing is reduced further all the models predict a substantial reduction in impact if the intervention fails to reduce sharing amongst new injectors. For example, if the frequency of syringe sharing is reduced by 75%, to an estimated four sharing events per month, the HCV sero-prevalence would reduce to 13–22% (amongst IDUs injecting for ≤8 years) if all IDUs were reached, whereas it would only reduce to 25–29% if recent IDUs were missed. Model B projects a much greater decrease in HCV sero-prevalence when all IDUs are reached because the model’s increased frequency of syringe sharing amongst new injectors initiates the HCV epidemic amongst the lower frequency syringe sharing IDUs, and so reducing syringe sharing in this period has a larger effect on the projected epidemic than for the other models.

**Impact of decreasing syringe sharing in low- or high-frequency syringe-sharing IDUs**

Figure 4 compares the impact of targeting higher frequency or lower frequency syringe sharers and shows that the impact of moderate decreases in syringe sharing is much greater if it is achieved in the low-frequency syringe sharing IDUs than if it was achieved in the higher frequency syringe sharing IDUs. Indeed, unless substantial decreases in sharing can be achieved in the higher frequency syringe sharers (>60%) little impact on HCV seroprevalence will be achieved unless the rest of the IDUs are also targeted. This is because of the high level of transmission occurring in the higher frequency syringe sharing IDUs.

**Discussion**

We developed a model of HCV transmission that incorporated key biological features of HCV infection and summary
Table 2 Behavioural and biological characteristics of the different classes/types of model fit. The table shows the parameter values for the best fits for each class

<table>
<thead>
<tr>
<th>Class of best-fit</th>
<th>Model projections</th>
<th>Behavioural model parameters</th>
<th>Biological model parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td>Factor increase in sharing rate</td>
<td>% of IDUs that share in the acute phase</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(syringe sharing rates are per month)</td>
<td>(injecting for less than four years)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean % of IDUs that resolve infection over 8 yrs</td>
<td>Mean % of IDUs that resolve infection over 8 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean chi-square error</td>
<td>Mean chi-square error</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td>1.0 (low)</td>
<td>1.0 (low)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.348</td>
<td>0.348</td>
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<tr>
<td></td>
<td></td>
<td>28.6%</td>
<td>28.6%</td>
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<tr>
<td>B</td>
<td></td>
<td>1.0 (low)</td>
<td>1.0 (low)</td>
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<tr>
<td></td>
<td></td>
<td>0.468</td>
<td>0.468</td>
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<td></td>
<td></td>
<td>26.3%</td>
<td>26.3%</td>
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<tr>
<td>C</td>
<td></td>
<td>1.0 (low)</td>
<td>1.0 (low)</td>
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<tr>
<td></td>
<td></td>
<td>0.457</td>
<td>0.457</td>
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<tr>
<td></td>
<td></td>
<td>35.0%</td>
<td>35.0%</td>
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<tr>
<td>D</td>
<td></td>
<td>2.7 (high)</td>
<td>2.7 (high)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.444</td>
<td>0.444</td>
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<tr>
<td></td>
<td></td>
<td>32.8%</td>
<td>32.8%</td>
</tr>
</tbody>
</table>

a The smaller the chi-squared error, the better the model fit.

b This is relative to the frequency of syringe sharing amongst the low-frequency syringe sharing IDUs.

c This is relative to the frequency of syringe sharing amongst the high-frequency syringe sharing IDUs.

IMPACT OF REDUCED SYRINGE SHARING ON HCV TRANSMISSION

The model accurately fitted the observed HCV seroprevalence in London (2002–03) by injecting duration. However, because of parameter uncertainty several different models, with contrasting biological and behavioural assumptions, gave equally good fits to the observed data. The key differences centred on how they simulated the rapid spread of HCV infection amongst new injectors, either assuming a large sub-group of high-frequency syringe sharing IDUs, increased syringe sharing among new injectors, or higher transmission during the acute infection phase. These models gave different projections for the proportion of IDUs with active HCV infection or that have resolved their infection (assumed to be immune), and the reduction in HCV seroprevalence in response to reductions in sharing.

Currently, there are insufficient data to determine which model type is the better description of HCV transmission in London, and probably also for other sites. Better information on several of the key biological or behavioural parameters could reduce the overall amount of parameter uncertainty and so improve model selection and the accuracy of projections. For example, if new experimental data strongly suggested that there was no increase in transmission risk during the acute phase of infection, then this could be ruled out as a possible reason for the rapid initial spread of HCV and one of our models could be rejected. Conversely, more accurate estimates for the proportion that resolve their infection could set stricter limits on estimates of syringe sharing.

Despite uncertainty in some important model parameters, the models provide a number of insights, highlighting the critical importance of reaching new injectors, and the potential difficulty in effectively controlling HCV transmission amongst IDUs, as highlighted by other modelling studies.38–40 Evidence suggests that the current level of intervention activity has been insufficient in preventing increases in HCV transmission in London.19,33,34 Because of this, the model was used to explore the possible impact of further reducing syringe sharing. The models project that if all IDUs reduce their syringe sharing the HCV seroprevalence in shorter term IDUs (injecting for less than four years) will be reduced, but that greater reductions are required to produce similar reductions amongst longer term IDUs (>eight years of injecting). In addition, and in agreement with a previous modelling study,28 the frequency of syringe sharing has to decrease to very low levels (one to two times per month) for the HCV seroprevalence to be reduced to ≤10%. Moreover, if interventions fail to reach recent injectors then the models project considerably smaller decreases in HCV seroprevalence. Targeting recent injectors may require the design of new interventions or innovative ways of delivery.

Lastly, as for sexually transmitted infection (STI) prevention interventions, one possible strategy for safer injecting and syringe distribution interventions could be to target higher risk IDUs. However, our model projections suggest that the most effective prevention strategy is to target all IDUs, rather than just higher frequency syringe sharers. Indeed, our model projections suggest that targeting higher risk IDUs could have less effect on the overall HCV seroprevalence than targeting lower frequency syringe sharers.
One potential limitation was that the model did not incorporate the possibility of HCV transmission through sharing other injecting equipment, primarily because of a lack of data. Equally, the model did not explicitly model periods of imprisonment when IDUs may have increased risk. The implication of these limitations is that the model may overestimate the impact of reducing syringe sharing on HCV prevalence. Critically, the analysis also lacked reliable data on the frequency and nature of syringe sharing, though not uncommon in behavioural surveys. We therefore combined information on injection frequency, syringe re-use and syringe coverage to provide an estimate of 16 sharing-events per month. The uncertainty in this parameter estimate was accounted for in the large uncertainty range given to the HCV transmission probability per syringe sharing act. Further, the model allowed for some heterogeneities in both syringe sharing (among recent or higher frequency syringe sharers) and the degree of mixing between different groups, but still assumed sharing was a random event. Clearly this is a simplification because syringe sharing, like drug taking, usually occurs within social groups and networks. We hypothesize that in the same way as concurrent sexual partnerships are important for STI spread, concurrent sharing partnerships formed in drug sharing networks may be important in determining the spread of HCV. However, such network effects cannot be incorporated and explored until better and more accurate data are collected on these risk behaviours.

**Figure 2** Projected HCV seroprevalence for different syringe sharing rates among IDUs who have been injecting for different durations. Figure 2a is for the best fit of class A, and 2b is for class B. The projections for class C are similar to class A. Class A and B models have similar characteristics except that class A has a larger sub-group of higher frequency syringe sharers (37% of IDUs) than class B (27% of IDUs) and new injectors in class B have an elevated syringe sharing rate (3.3 times higher than other IDUs) but do not in class A.
Figure 3 Impact on endemic HCV seroprevalence of reducing syringe sharing amongst all IDUs, or IDUs who have been injecting for >1 year. Projections are shown for the best-fit models of class A, B and C, and the HCV sero-prevalence is the average over all IDUs who have been injecting for ≤8 years. Class A, B and C models have similar characteristics except that class A and C have a larger sub-group of higher frequency syringe sharers (37 and 47% of IDUs for A and C respectively) than class B (27% of IDUs), a higher proportion of infecteds resolve infection in class A and B (41–47%) than in class C (18%), and new injectors in class B have an elevated syringe sharing rate (3.3 times higher than other IDUs) but do not in class A or C.

Figure 4 Impact on the endemic HCV seroprevalence of reducing syringe sharing amongst high and low frequency syringe sharing IDUs. Projections are shown for the best-fit models of class A, B and C, and the HCV sero-prevalence is the average over all IDUs who have been injecting for eight years or less. Class A, B and C models have similar characteristics except that class A and C have a larger sub-group of higher frequency syringe sharers (37 and 47% of IDUs for A and C respectively) than class B (27% of IDUs), a higher proportion of infecteds resolve infection in class A and B (41–47%) than in class C (18%), and new injectors in class B have an elevated syringe sharing rate (3.3 times higher than other IDUs) but do not in class A or C.

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References


Appendix

Appendix 1 Flow diagram for HCV transmission model. Arrows portray possible transformations of susceptible or infected IDUs, and the parameters next to these arrows are the rate of flow per capita between these states.