In a number of countries, injecting of illicit drugs has been recognized as an important pathway for the transmission of blood-borne viruses. Of particular concern have been epidemics of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) infection among drug users, arising through the sharing of equipment used in injecting. In many parts of the world, the prevalence of HIV infection among people who inject drugs has risen to 40–60% in the space of a few years. Hepatitis C virus prevalence has generally been found to be at least 50% in this population. As the parenteral route is the dominant mode of transmission of HCV, and a major source of HIV infection, the avoidance of sharing injecting equipment can have a large impact on reducing the spread of HIV and HCV.

There has been considerable debate about the value of needle and syringe distribution programmes, and the impact of other approaches to reducing the risk of blood-borne virus transmission among injecting drug users (IDU). Epidemiological studies of the effect of prevention activities are very difficult to carry out in this population, because of the challenges of follow-up and confounding. Mathematical modelling provides an alternative means of obtaining insight into the dynamics of viral transmission among IDU, including the consequences of specific interventions in this population. A number of authors have used this approach over the past decade. Kaplan uses a model with two differential equations describing prevalence and the probability of infection for HIV, where sharing occurs only in shooting galleries. Greenhalgh & Hay extend Kaplan’s model to allow some different behaviour in the rate of visitation of shooting galleries and the likelihood of infection. Peterson et al. use a Monte Carlo approach. Massad et al. develop a dynamical model that tracks HIV-infected needles and their interaction with infected and uninfected IDU. Iannelli et al. use a contact model that does not explicitly parameterize sharing. Kretzschmar & Wiessing require the specification of an underlying social network. The most extensive model is by Blower et al. This dynamical model investigates HIV infection through heterosexual and IDU contact for IDU in New York city. It allows contact through buddy and stranger user groups and is

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DYNAMICS OF HIV AND HCV AMONG IDU

Materials and Methods
The mathematical model

A mathematical model is constructed using differential equations. By definition the term IDU refers to only current IDU. For an infection of interest (HIV or HCV in this case), the model describes \( I(t) \), the number of current IDU who have the infection at time \( t \). This number changes over time, according to the rate at which new infections occur in this population, and the rate at which those with infection leave the population, either through death, or by stopping the practice of injecting drugs.

New infections can either occur through the reuse or sharing of equipment, or through other routes such as sexual transmission. Sharing refers to all equipment related to drug use. There is some evidence that equipment such as swabs, tourniquets, and even table-tops can be important in HCV transmission. However their effect is considerably smaller than transmission through shared needles.\(^{11}\) Sharing also refers to re-use of needles, as these are the dominant transmission vehicle, over extended periods of time. Access to clean needles from Needle Exchange Programs in Australia implies that the majority of sharing will occur in a single injecting episode.

The number of new infections at time \( t \) occurring through sharing is assumed to be proportional to the number of current infected IDU in the population. The process can be described graphically as in Figure 1, where \( aI \) is the average rate of new infections per year from needle sharing, \( bI \) is the average rate per year of loss of infected IDU through all means, and \( c \) is the rate of new infections per year from non-needle sharing means.

The differential equation for this process has the form

\[
\frac{dI}{dt} = aI - bI + c \quad \text{(Eqn 1)}
\]

A key measure of the impact of transmission is the prevalence of viral infection among IDU. If the total population of IDU, with and without infection, is represented by the function \( U \), then the prevalence at any point in time is given by \( a(t) = I(t)/U(t) \).

The parameter \( a \) defines the number of new infections per time period that will be transmitted from each currently infected IDU via sharing. It can be represented as

\[
a = p(1 - d)m(n,a) \quad \text{(Eqn 2)}
\]

where \( p \) is the probability of infection through a single reuse of contaminated equipment by a previously uninfected person, \( n \) is the average number of IDU using the same equipment at a given episode of injecting, \( m \) is the average number of injecting episodes per year for an IDU, \( d \) represents the fraction of needles that are cleaned before use, and \( u \) is the number of uninfected IDU who are at risk of infection through needle contact per infected IDU per injection. When the prevalence of infection in a population is still low, the functional form of \( u \) ([Eqn A1], Appendix),

\[
u = n - \frac{n\alpha(n + 1)}{1 - (1 - \alpha)^n + n\alpha} \quad \text{(Eqn 3)}
\]

simplifies to

\[
u_{\text{low}} = \frac{n - 1}{2} \quad \text{(Eqn 4)}
\]

This result can be understood by noting that when prevalence is low, only one of the \( n \) users will generally be infected and, on average this person will fall in the middle of the sequence of reusing. Consequently only the \((n - 1)/2\) users that follow the infected person are at risk of infection.

Critical levels of drug injecting

Containing or reducing total infection numbers depends primarily on the relative sizes of \( a \) and \( b \) in (Eqn 1). If \( a \) is always less than \( b \) then infected levels will be maintained solely by input from non-needle sharing \( c \). We define the critical sharing level \( s_c \) to be the amount at which new infections through sharing can start to increase infection levels beyond that arising from other sources. This occurs when the maximum value of \( a \) equals \( b \). As \( a \) is a decreasing function of prevalence, the maximal value of \( a \) occurs at low prevalence and is given, according to (Eqn 4), by \( a_{\text{max}} = p(1 - d)m(n - 1)/2 \).

For each IDU, the number of people that person has shared needles with over the course of a year is given by \( m(n - 1) \). The critical sharing level for incidence, \( s_{\text{ci}} = m_{\text{n}}(n - 1) \), is determined when

\[
b = a_{\text{ci}} = p(1 - d)m_{\text{n}}(n - 1)/2
\]
Hence

\[ s_{cp} = m_{cp}(p_{cp} - 1) = \frac{2b}{p(1 - d)} \]  
(Eqn 5)

Critical sharing levels for prevalence, \( s_{cp} \), are calculated in the same manner but now we must also include the ‘loss’ of the proportion of IDU that are infected through any growth in total IDU numbers. Hence the derivation above follows the same steps but with now the loss term \( b \) replaced by \( b + r \), where \( r \) assesses the annual rate of increase of total IDU numbers. The critical sharing level for prevalence, \( s_{cp} \), is then

\[ s_{cp} = m_{cp}(p_{cp} - 1) = \frac{2(b + r)}{p(1 - d)} \]  
(Eqn 6)

### Table 1: Literature estimates of parameter values and bounds

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
<th>Value</th>
<th>Bounds</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>( p_{HIV} )</td>
<td>Risk of HIV(^a) per injection with an infected needle before 1994, and by 1999</td>
<td>0.02, 0.72 x 0.02</td>
<td>[0.003, 0.033]</td>
<td>0.3% risk through percutaneous HIV exposure,(^{1,7}) 3.3% of health workers exposed to HIV infected through hollow bore needles in 1995;(^{16})</td>
</tr>
<tr>
<td>( p_{HCV} )</td>
<td>Risk of HCV(^b) per injection with an infected needle</td>
<td>0.04</td>
<td>[0.012, 0.1]</td>
<td>1.2% of health workers infected with HCV through hollow bore needles;(^{18}) 10% maximum risk of HCV through needle-stick injury;(^{19}) 4% average HCV infections from hollow bore needle accidents;(^{16})</td>
</tr>
<tr>
<td>( d )</td>
<td>Fraction of needles cleaned before use in 1980, 1988, 1994</td>
<td>0, 0.2, 0.5</td>
<td>[0.5(d), 1.5(d)]</td>
<td>10% average cleaning of needles in 1986, 47% in 1988, and range of 33% to 77% in 1994;(^{20})</td>
</tr>
<tr>
<td>( f )</td>
<td>Cleaning effectiveness against HCV relative to HIV</td>
<td>0.25</td>
<td>[0.1, 0.75]</td>
<td>HCV contaminated equipment besides needles;(^{11})</td>
</tr>
<tr>
<td>( m )</td>
<td>Number of injections per year. Independent values allowed in 1980, 1985, 1988, 1994</td>
<td>60</td>
<td>[0.5(m), 1.5(m)]</td>
<td>94% (19%) shared needles in preceding month in 1985 (1994);(^{20}) 23% of IDU(^c) at Needle Exchange Programs used needles after someone else in 1999;(^{14}) Appendix</td>
</tr>
<tr>
<td>( n )</td>
<td>Average number of people using equipment per injecting episode in 1985 and 1994</td>
<td>1.2, 1.1</td>
<td>1 + [0.5((n - 1), 1.5(n - 1)]</td>
<td>94% (19%) shared needles in preceding month in 1985 (1994);(^{20}) 23% of IDU(^c) at Needle Exchange Programs used needles after someone else in 1999;(^{14}) Appendix</td>
</tr>
<tr>
<td>( b_{HIV} )</td>
<td>Rate at which IDU with HIV infection leave the IDU population before 1995 and in 1999 with HAART(^d)</td>
<td>0.11, 0.05 + 0.2 x 0.06</td>
<td>[0.05, 0.15]</td>
<td>14,21,22 5% loss of IDU from stopping injecting,(^{21,22}) with 6% loss due to death from HIV early in infection with this decreasing from 1994 to 20% of this death rate in 1999 due to HAART;(^{16})</td>
</tr>
<tr>
<td>( b_{HCV} )</td>
<td>Rate at which IDU with HCV infection leave the IDU population</td>
<td>0.05</td>
<td>[0.03, 0.07]</td>
<td>14,21,22 5% loss of IDU from stopping injecting,(^{21,22}) with 6% loss due to death from HIV early in infection with this decreasing from 1994 to 20% of this death rate in 1999 due to HAART;(^{16})</td>
</tr>
<tr>
<td>( \epsilon_{HIV} )</td>
<td>Annual number of new HIV infections from non-needle sharing in 1985 and 1994</td>
<td>100, 20</td>
<td>[0.5(\epsilon_{HIV}), 1.5(\epsilon_{HIV})]</td>
<td>Equivalent rates of new HIV infection through injecting drug use, and male homosexual contact and injecting drug use,(^{14}) and estimated injecting drug use incidence;(^{14})</td>
</tr>
<tr>
<td>( \epsilon_{HCV} )</td>
<td>Annual number of new HCV infections from non-needle sharing in 1990</td>
<td>300</td>
<td>[0.5(\epsilon_{HCV}), 1.5(\epsilon_{HCV})]</td>
<td>This represents 6% of all HCV incidence,(^{13}) in the range of observed values of 4% to 12%;(^{11})</td>
</tr>
</tbody>
</table>

\(^a\) Human immunodeficiency virus.

\(^b\) Hepatitis C virus.

\(^c\) Intravenous drug user.

\(^d\) Highly active antiretroviral therapy.
Availability of highly active antiretroviral therapy (HAART) in Australia in 1995 has led to lower viral levels in individuals with HIV infection. Accordingly the HIV transmission probability $p_{HIV}$ will have decreased with time. The pre-1995 value of $p_{HIV}=0.02$, combined with the expected proportion of individuals with HIV RNA copies per ml in three viral groups, $<400$, $400–10\,000$, and $>10\,000$ (determined from those proportions of individuals in 1999 receiving no treatment\(^1\)), and assuming each log$_{10}$ drop in viral levels reduced probability of infection by 2.45\(^2\), provided probabilities of HIV transmission in each of these groups. The expected probability of HIV transmission in recent times was then determined from the proportion of individuals in 1999 under all treatment types, including no therapy, in each of these three viral groups, and their individual probabilities. This calculation led to $p_{HIV}$ reducing to 72% of its initial level by 1999. This may be an overestimate of the reduction as the calculations were performed on values from individuals registered on the Australian HIV Observational Database that may underestimate untreated individuals.

**Sensitivity analysis**
Sensitivity to parameter values was determined by the Monte Carlo method using 1000 simulations. Each parameter was assigned a Beta distribution with the parameter value from Table 1 taken as the most likely estimate and the bounds providing 6 SD, so at least 90% CI. Prevalence and incidence values were calculated at 5-yearly intervals for each simulation.

**Results**

**Simulation of human immunodeficiency virus prevalence among injecting drug users in Australia**
The model of prevalence dynamics among IDU, and the parameter choices in Table 1, produce the prevalence levels shown in the top left plot in Figure 2, along with the range of values for the Monte Carlo simulations. Incidence rates are plotted against literature estimates in the bottom left plot of Figure 2. The incidence rates model literature estimates closely. In 1997 prevalence was estimated at 0.9% for attendees at Needle Exchange Programs\(^3\). Our simulations provide an estimate of 0.2% prevalence over all IDU.

![Figure 2](https://academic.oup.com/ije/article-abstract/32/5/708/665704 by guest on 18 April 2019)

Figure 2 Prevalence and incidence rates\(^3,\!^4\) over time for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) (solid lines). The $\times$ in HIV incidence depict literature estimates. In HCV incidence plot, the dashed line shows best estimates of HCV incidence from the literature, and the dotted lines show upper and lower estimates. Included boxplots show range of values with 1000 Monte Carlo simulations, the central bar denoting the median, the box giving the interquartile range.
Simulation of hepatitis C virus prevalence among injecting drug users in Australia

Evidence for the HCV epidemic among IDU in Australia points to its outbreak in the late 1950s. Beginning our simulation in 1960 produces the prevalence and incidence levels shown in the two right hand plots in Figure 2. The HCV prevalence levels for people attending needle and syringe exchange programmes were 63% in 1995, 51% in 1996, and 50% in 1997.14 Our simulated values provide a reasonable approximation to these figures especially since the data is more likely to represent regular IDU rather than all IDU as here. The simulations also duplicate the decreasing trend for prevalence with increasing incidence.

Critical human immunodeficiency virus sharing

With current values for sharing and cleaning, an assumed 5% annual increase in the number of IDU, and estimated reduction in HIV transmission probability and death due to HAART, we obtain $s_{0,p} = 31$, so that on average every IDU would need to share with 31 others over a year before HIV prevalence would be in danger of rising to significant levels. Current sharing estimates are $s = m(n - 1) = 6$. We would need a fivefold increase in sharing before this critical level was breached and prevalence started to rise to significant levels in the entire IDU community. The critical sharing level for total infected numbers is 17. Without HAART, the critical sharing level for infected numbers would be higher at 22, due mainly to the faster removal through HIV mortality.

Critical hepatitis C virus prevalence

The critical sharing level for HCV prevalence is 5.7, suggesting that HCV prevalence will stay elevated. Although prevalence is seen to fall in the simulation, it will stay above 25% in the long term. Critical sharing level for infected numbers is below 3 and so a more significant decrease in current sharing is required for absolute numbers of HCV-infected IDU to fall.

Harm reduction

The model equations ([Eqn 1], [Eqn 2], [Eqn 3]), can be modified to incorporate the effects of harm reduction strategies. If a proportion $\gamma$ of infected IDU know they are infected and use injection equipment last, then the expression for $u$ in (Eqn 3) changes to $u = \left(1 - \gamma\right)^{(n - m)\alpha(1 - \gamma) + 1}\left(1 - \left(1 - \alpha\right)r + m(1 - \gamma)\alpha\right)$. If this harm reduction strategy is effected from 2000, then for $\gamma = 0.2$ and $\gamma = 0.5$ there will be little reduction in HIV prevalence as its main source is from non-sharing sources, and a reduction in HIV incidence in 2005 from 9 to 8 and 6 respectively. However, these strategies may achieve an estimated reduction in HCV prevalence from 32.7% with no harm reduction to 31.3% and 28.7% respectively in 2005. Hepatitis C virus incidence may be reduced from 13 400 in 2005 to 11 600 and 8300 respectively.

Discussion

There has been continuing debate in Australia regarding the effectiveness of needle and syringe exchange programmes, along with other preventive programmes aimed at reducing transmission of infectious diseases among IDU, in the face of the qualitatively very different HIV and HCV epidemics in IDU. These programmes appear to have been very effective at limiting the spread of HIV among IDU in Australia, but ineffective at avoiding or markedly reducing the very large HCV epidemic in IDU. Our model confirms one suggestion made elsewhere11 that these qualitatively very different epidemics can be explained in terms of the greater HCV infectivity, expressed here through the higher transmission probability $P_{HCV}$ and the less-effective cleaning of HCV-contaminated equipment.

The advantages of modelling HIV and HCV simultaneously is that it provides tighter estimation of the parameters and hence is likely to be more precise in the source of their differences. The majority of the rise in HIV prevalence in IDU is due to infection from non-needle sharing means. The sudden drop in incidence after the peak reflects the impact of the needle exchange programmes and resulting lower sharing of needles.

Needle exchange programmes also affected HCV prevalence and incidence but to a lesser extent. It caused a drop in prevalence but could only stabilize incidence. Hepatitis C virus is more infectious than HIV through needle sharing and so we would expect a lower impact on HCV profiles with reduced sharing and more cleaning.

Clearly there are limitations inherent in the model we have developed. One major limitation is that it assumes a homogeneous group. Although HIV and HCV viral levels differ substantially during the course of infection, no variability in transmission dynamics was included. Due to the limited data available however, our approach here has been to develop a relatively simple model of overall injecting behaviour. Subject to these limitations, the model provides a means of estimating the development of infection levels when injecting behaviour changes. In particular, it provides an estimation of the critical sharing level, that level that divides cases of minimal prevalence from possibly high levels. Defining the sharing level to be the number of people an IDU shares with over a year, we find that the critical sharing level for HIV prevalence is 31, whereas the current estimated sharing level is 6, providing a reasonable buffer before HIV prevalence increases. This explains the low prevalence of HIV in the Australian IDU community. We must recognize that these calculations treat the IDU community as a homogeneous group. Although sharing levels are below the critical level for this group, there will be subgroups, in particular regular IDU concentrated in single geographical areas, which will be closer to or may exceed their own critical sharing level. Assuming the number of annual injecting episodes is 200, a level more indicative of regular IDU, leads to simulated HIV prevalence in 1997 of 1.3%, consistent with the 0.9% observed HIV prevalence in that year among attendees at Needle Exchange Programs.16 If the number of annual injecting episodes rises to 310 so that $m(n - 1)$ equals the critical sharing level for prevalence, then HIV prevalence reaches 4% in 2005.

Highly active antiretroviral therapy has impacted on the dynamics of HIV infection in the general and IDU communities. We have estimated that it has lowered HIV transmission probability per single contact with an HIV-contaminated needle to approximately 70% of the pre-HAART risk, due to lower average HIV RNA levels in peripheral blood. On the other hand, HAART has increased the number of HIV IDU through reduced mortality. These competing effects have led to higher risk as the
80% reduction in HIV progression outweighs the benefits of reduced transmission probability. The effect can be seen in critical HIV sharing level for incidence being reduced from 22, assuming no HAART, to its estimated value of 17 with HAART.

For HCV the critical sharing level for prevalence is 5.7, less than current estimates of sharing. The critical sharing level for the number of HCV-infected IDU is below 3, suggesting that sharing will need to halve if HCV incidence is to decrease substantially. The lower needle sharing has caused a drop in prevalence levels over recent years. However, as the current sharing level exceeds the critical sharing levels for both prevalence and number, the percentage and number of HCV-infected IDU will remain significant. The interquartile ranges of HCV prevalence and incidence show substantial infection, a marked contrast to the HIV scenarios (Figure 2). This provides further indication that HCV will remain a significant health problem among IDU in Australia, even with lower risk behaviour.

Harm reduction strategies can reduce transmission through needle sharing. Since HIV prevalence is low and supported mainly by new infections from non-sharing sources there will be little impact on HIV prevalence and incidence. For HCV there can be a marked reduction. If 20% (50%) of HCV-infected IDU know they are infected and share equipment last, with this behaviour beginning in year 2000, then in 2005 HCV prevalence will reduce from 32.7% with no harm reduction to 31.3% (28.7%). The HCV incidence will reduce from 13 400 to 11 600 (8300). However, this may be an overestimate of effectiveness as HCV can be transmitted from other contaminated equipment in the immediate environment.

Although this model has been applied to the Australian IDU community, it is equally applicable to other communities. The model provides a means of estimating future, and current, infection levels. It estimates critical sharing levels, presenting a well-defined goal for health authorities to achieve significant reduction in infection levels.

**KEY MESSAGES**

- A mathematical model was developed to study human immunodeficiency virus (HIV) and hepatitis C virus (HCV) dynamics in the injecting drug user community in Australia.
- Simulations indicate that under current behaviour HIV prevalence will remain low in this group but that HCV prevalence will stay elevated.
- Our calculations suggest that a halving of sharing is needed for HCV prevalence to fall significantly.

**References**

Appendix

The rate of infection through needle sharing

Let $\alpha$ be the probability that an IDU is infected. Define $\hat{u}$ to be the expected number of uninfected IDU that will use a needle after an infected IDU. If $n$ people use a single needle, and there are $\hat{n}$ of these who are infected, then these $\hat{n}$ should be equally distributed among the $n$ on average. We can consider every uninfected person using the needle after the first infected person to be at risk of infection. Then $\hat{u}$ is given by the number of uninfected persons using a needle $n - \hat{n}$ multiplied by the proportion of these that follow the first infected person $\hat{n}/(\hat{n} + 1)$. Hence

$$\hat{u} = \frac{(n - \hat{n})\hat{n}}{n + 1}$$

Before we use this to obtain $\alpha$, which is the rate of new infection from needle sharing per infected IDU, we must adjust it for multiple counting. As there can be more than one infected IDU in the group of $n$ we must divide $\hat{u}$ by the expected number of infected IDU (given that there is at least one) among the $n$. Let $z$ represent the random variable of the number of infected people sharing a needle. We need to determine $\hat{n} = E[z \mid z \geq 1]$. Let $E[z \mid z \geq 1] = E[z]/P(z \geq 1) = \frac{n\alpha}{(1 - (1 - \alpha)^n)}$

Therefore $u$, the expected number of uninfected IDU that are at risk of infection through needle contact, per infected IDU, per single needle, is given by

$$u = \frac{\hat{u}}{E[z \mid z \geq 1]} = \frac{n - \hat{n}}{n + 1} = n - \frac{n\alpha(n + 1)}{1 - (1 - \alpha)^n + n\alpha} \quad \text{(Eqn A1)}$$

For low $\alpha$, the term $(1 - \alpha)^n$ can be approximated by $1 - n\alpha$ so that the expression for $u$ in (Eqn A1) can be replaced by

$$u_{low} = \frac{n - 1}{2}$$

Calculation of needle sharing in Australia

Let the random variable $N(t)$ represent the number of times an IDU used a needle after another IDU in $t$ years. We assume this has a Poisson distribution with an expected value for $t = 1$ of $\bar{m} = \min(m(n - 1)/2, m)$ where $m$ is the number of injections per year for an IDU, and $\min$ takes the minimum of the two values.

The assumption underlying $\bar{m}$ is that if the average number of people that share a needle, $n$, is large then approximately every injection per year will be shared and $\bar{m} = m$; on the other hand if few people share a needle on average, so that $n < 2$, then $\bar{m} = m(n - 1)/2$, where we divide by 2 because if only 2 people share a needle only one of those will use it after another. The probability that an IDU does not use a needle after another for one month is then $P(N = 0, t = 1/12) = e^{-\bar{m} t/12}$. Estimates of this value can be obtained from ref. 14. In 1999 the proportion of IDU sharing a needle in a preceding month within Australia was 23%. Therefore for that year $e^{-\bar{m} t/12} = 1 - 0.23$. Since the level of sharing is not too large we can replace $\bar{m}$ with $m(n - 1)/2$ to obtain

$$m(n - 1)/2 = -12\ln(0.77) = 3.1$$

Therefore we have $m(n - 1) = 6$. We use the value $m = 60$ for all relevant times and so we assume $n = 1.1$ for 1994 and later. Choices of other pairings provided roughly equivalent results. The value of $n$ before 1985 was chosen to be consistent with 40% sharing in 1985.14