The Impact of Needle and Syringe Programs on HIV and HCV Transmissions in Injecting Drug Users in Australia: A Model-Based Analysis

Jisoo A. Kwon, BSc, Jenny Iversen, Lisa Maher, PhD, Matthew G. Law, PhD, and David P. Wilson, PhD

Objectives: We aim to estimate how changes in sterile syringe distribution through needle–syringe programs (NSPs) may affect HIV and hepatitis C virus (HCV) incidence among injecting drug users (IDUs) in Australia.

Methods: We develop a novel mathematical model of HIV and HCV transmission among IDUs who share syringes. It is calibrated using biological and Australian epidemiological and behavioral data. Assuming NSP syringe distribution affects the number of times each syringe is used before disposal, we use the model to estimate the relationship between incidence and syringe distribution.

Results: HIV is effectively controlled through NSP distribution of sterile syringes {with the effective reproduction ratio below 1 [0.66 median, interquartile range (0.63–0.70)] under current syringe distribution}. In contrast, HCV incidence is expected to remain high and its control is not feasible in the foreseeable future. The proportion of injections that are shared and the number of times each syringe is used before disposal are the driving factors of HCV incidence. The frequency in which each syringe is used can potentially be influenced by changes in syringe distribution. We estimate that if syringe distribution or coverage doubled, then annual incidence is likely to reduce by 50%. However, if it was decreased to one third of the current level, then ~3 times the incidence could be expected.

Conclusions: This research highlights the large benefits of NSPs, puts forward a quantitative relationship between incidence and syringe distribution, and indicates that increased coverage could result in significant reductions in viral transmissions among IDUs.

Key Words: Australia, HCV, HIV, injecting drug users, mathematical model, needle and syringes

(*J Acquir Immune Defic Syndr* 2009;51:462–469)

Received for publication August 14, 2008; accepted February 5, 2009.

From the National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Sydney, New South Wales, Australia.

Supported by Australian Research Council (DP0771620). The National Centre in HIV Epidemiology and Clinical Research is funded by the Australian Government Department of Health and Ageing and is affiliated with the Faculty of Medicine, University of New South Wales.

All authors have no conflicts of interest.

Correspondence to: David P. Wilson, PhD, National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, Level 2, 376 Victoria Street Darlinghurst, Sydney, New South Wales 2010, Australia (e-mail: dwilson@nchecr.unsw.edu.au).

INTRODUCTION

Sharing syringes by injecting drug users (IDUs) is an important mode of global transmission of blood-borne viruses such as HIV and hepatitis C virus (HCV).[1] Both HIV and HCV infection are associated with significant morbidity and mortality.[2,3] In Australia, HCV is highly prevalent in IDUs (50%–70%),[4–7] but HIV has remained consistently low (prevalence of <1%).[4–8] Annually, there are 30–40 notified cases of HIV transmission in Australia attributed solely to injecting drug use.[3] In comparison, there are an estimated 8000–12,000 new HCV infections annually,[3,9] 80%–90% of which are attributed to injecting drug use.[6,10,11] Similar proportions of HCV transmissions worldwide are observed in IDUs.[12,13] In contrast, the majority of HIV transmissions globally occur as a result of unprotected heterosexual or male homosexual intercourse.[2,14] This is due to the differential transmission probabilities of the 2 viruses.[15] Despite the difficulty in estimating transmission risk, the per exposure probability of infection from a contaminated syringe is thought to be 0.1%–0.5% for HIV[16–23] and 2.5%–5% for HCV.[24–28]

Transmission via a contaminated syringe can occur when syringes are shared among IDUs. Although IDUs are unlikely to share or reuse other injector's used syringes, if they have convenient access to clean syringes,[29,30] those who do share syringes tend to share with sexual partners or close friends.[31,32] In Australia, needle and syringe programs (NSPs) have been the cornerstone of public health strategies aimed at reducing the sharing of syringes. NSPs were first introduced in Australia in the late 1980s, providing a range of education, counseling, and referral services alongside the distribution of sterile injecting equipment. Initially, NSPs were established to prevent transmission of HIV, but since the 1990s, prevention of HCV among IDUs has also been a key objective. There are over 3000 NSP sites across Australia, with the sector comprised of primary and secondary NSP outlets, mobile and outreach services, syringe vending machines, and a significant number of pharmacies that offer NSP services.[33] The combined needle and syringe distribution is ~30 million syringes each year.[9] It has been estimated that by the year 2000, Australian NSPs had directly prevented 25,000 cases of HIV and 21,000 cases of HCV.[34] In this article, we develop a novel mathematical model, calibrated to match the Australian population of IDUs, and we use it to estimate the relationship between the number of sterile syringes distributed through NSPs and the expected incidence of HIV and HCV in Australian IDUs.

METHODS

Various studies have used mathematical models to evaluate interventions designed to control and prevent viral transmission among IDUs.[16,35–44] We developed a simple but novel static model to explore the expected national annual incidence associated with different levels of sterile syringe distribution. A schematic diagram describing the assumptions and structure of our transmission model is presented in Figure 1.

We define the number of IDUs in the population as N and assume that each IDU injects an average of n times per year. A proportion, s, of IDUs may share their syringes with others and they do so in a proportion, q, of their injections. We assume that sharing occurs in sharing groups of average size m people. We define the prevalence in the population to be p_0 and the probability of infection from a contaminated syringe per use to be β. We assume that syringe cleaning has effectiveness ε_c and that cleaning occurs before a proportion, p_c, of shared injections. Given these definitions, the average number of "sharing events" in total per year is $\frac{\mathrm{N}nsq}{m}$. The total number of expected transmissions will be this number multiplied by the average number of transmissions per "sharing event". The probability of r infected people in a sharing group of size m is $\binom{m}{r} p_0^r (1-p_0)^{m-r}$, using standard binomial theory (p_0 will take different values depending on whether HIV or HCV is modeled). If the group members inject using the shared syringe in random order, then an average of $\frac{m-r}{r+1}$ uninfected people will inject before the first infected person (and between each infected person). Therefore, in each sharing event, an average of $m - \frac{m-r}{r+1} - r = \frac{rm-r^2}{r+1}$ uninfected people will use a syringe after an infected person has used it. If a shared syringe is used δ_s times before disposal, then m/δ_s syringes are used in each "sharing event" and the average number of uninfected people in the group to use the same syringe after an infected person becomes $\frac{rm-r^2}{r+1}\frac{\delta_S}{m}$. Each susceptible person could acquire infection with probability $(1-p_c\varepsilon_c)\beta$. Therefore, the expected number of transmissions in the sharing group is:

$$\frac{\delta_S \beta (1-p_c\varepsilon_c)}{m} \sum_{r=1}^{m-1} \binom{m}{r} p_0^r (1-p_0)^{m-r} \frac{rm-r^2}{r+1}.$$

We note that $\delta_s \geq 2$ because sharing events necessarily involve sharing syringes. We assume that syringes used for personal (unshared) injections are each used an average of δ_p times before disposal. Then the total number of transmissions expected each year or incidence (I) is

$$I = \frac{\mathrm{N}nsq\delta_S \beta (1-p_c\varepsilon_c)}{m^2} \sum_{r=1}^{m-1} \binom{m}{r} p_0^r (1-p_0)^{m-r} \frac{rm-r^2}{r+1} \quad (1)$$

If each IDU injects for an average of D years after seroconversion, then the average number of secondary cases per IDU is

$$R = \frac{Dnq\delta_s \beta (1-p_c\varepsilon_c)}{m^2 p_0} \sum_{r=1}^{m-1} \binom{m}{r} p_0^r (1-p_0)^{m-r} \frac{rm-r^2}{r+1}.$$

It is assumed that the saturation in demand has not been reached and greater supply would result in greater coverage. If P syringes are distributed each year and a proportion ω of all syringes are not used, then the number of syringes distributed that are used is $P(1-\omega)$. The number of syringes used for individual injecting episodes among nonsharing IDUs is $\frac{n\mathrm{N}(1-s)}{\delta_p}$. Similarly, the total number of syringes used for individual injecting among all sharing IDUs is $\frac{n(1-q)s\mathrm{N}}{\delta_p}$ and the total number of syringes used in sharing events is $\frac{nqs\mathrm{N}}{2\delta_s}$. Therefore,

$$P(1-\omega) = \frac{n\mathrm{N}(1-s)}{\delta_p} + \frac{n(1-q)s\mathrm{N}}{\delta_p} + \frac{nqs\mathrm{N}}{\delta_s} = \frac{n\mathrm{N}}{\delta_p\delta_s}\left[\delta_s - sq(\delta_s - \delta_p)\right] \quad (2)$$

defines a relationship between the total number of syringes distributed and the use of syringes in our model (Fig. 1). Changes in the number of syringes distributed are likely to change any, or all, of the following factors in a way that is consistent with equation 2: the proportion of syringes that remain unused (ω), the proportion of injections that are shared (q), or the average number of times each syringe is used [in shared (δ_s) or individual (nonshared) injections (δ_p)]. Changes to ω and δ_p will not influence transmission levels but changes to q and δ_s could potentially result in large changes in incidence. We speculate that increased syringe coverage is most likely to influence a decrease in the number of injections per syringe (for both personal and shared syringes). Therefore, we used equation (2) to estimate the change in the average number of injections per syringe used in both individual and shared injections, assuming the same percentage increase or decrease for both, according to a change in the total number of syringes distributed. The new values for the usage per syringe (δ_p and δ_s) were then used in equation (1), and all other parameters were sampled independently from their original distributions as defined in Table 1. This was used to estimate the expected incidence of HIV and HCV based on changes in syringe distribution.

We acknowledge that there is large heterogeneity in the behavior of different IDUs. However, in this study, we take population averages to investigate expected population-level incidence based on average parameter estimates. Parameter estimates used in our model are presented in Table 1. Because of the uncertainty and heterogeneity in these parameters, we defined a range of plausible values. We sampled each parameter over a uniform distribution using Latin hypercube sampling and conducted sensitivity analyses using the SaSAT software package.[51] For illustrative purposes, we used median parameter values for the generation of some figures. We used the same behavioral parameters for both epidemics but changed the biological transmission rate per exposure for each virus, 0.1%–0.5% for HIV and 2.5%–5% for HCV,[16–28] and the baseline prevalence of HIV and HCV in the Australian IDU population, 0.5%–1.5% for HIV and 50%–70% for HCV.[4–8] These parameter values ensured that the model was calibrated to accurately reflect the number of notifications recorded in Australia each year; the model estimated that 34 [median, interquartile range (IQR) (11–75)] HIV infections and 10,268 [median, IQR (5884–15,192)] HCV infections

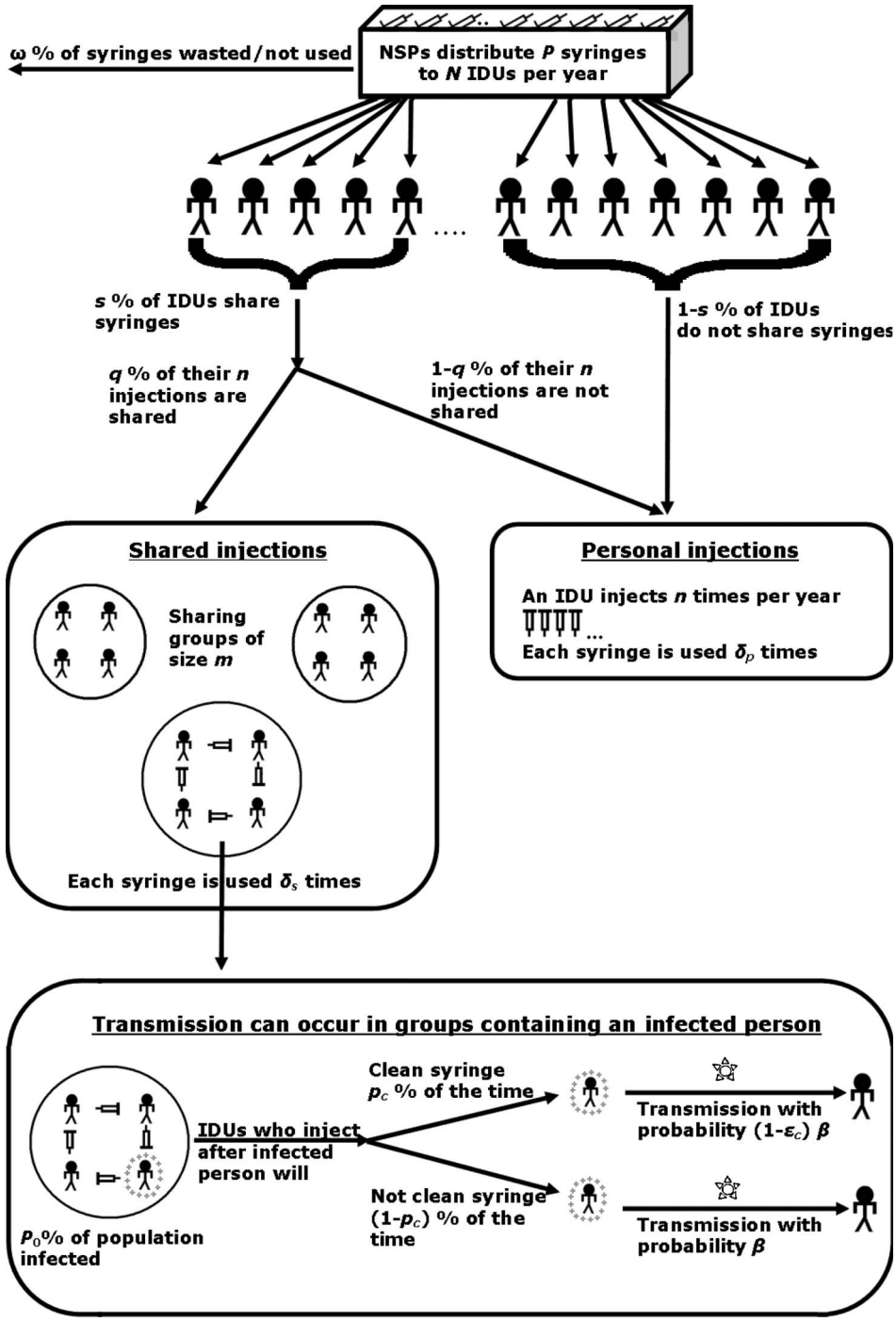

FIGURE 1. Schematic diagram of the injecting patterns of IDUs. An IDU with cross mark refers to an infected IDU in a sharing group. A star from an infected IDU to an uninfected IDU refers to the transmission of HIV and HCV virus through a contaminated syringe via needle sharing.

occur each year, which is consistent with national annual notifications data.[3,52]

RESULTS

The total number of secondary transmissions resulting from an infected IDU depends on the frequency of syringe sharing and the average duration of time IDUs inject postseroconversion. We calculated the expected reproduction ratio, R, per IDU for HIV and HCV as a function of the average duration of injecting postseroconversion (Fig. 2). An epidemic is sustained if R is greater than 1,[53] implying that each infected person is associated with at least 1 secondary transmission on average. We found that the threshold duration of injecting postseroconversion required to sustain an epidemic is 11.6 [median, IQR (7.0–22.4)] years for HIV and 2.3 [median, IQR (1.8–3.2)] years for HCV (Fig. 2). Based on behavioral data,[4,54] it is reasonable to assume that the average duration of

TABLE 1. Table of Parameters Used in Mathematical Model of Transmission Among IDUs in Australia

Parameter	Description		Values	References
Biological transmission parameters				
β	Transmission probability per injection with a contaminated syringe	HIV	0.001–0.005	16–23
		HCV	0.025–0.05	24–28
Epidemiology and NSP parameters				
p_0	Prevalence among IDUs in Australia	HIV	0.5%–1.5%	4–8
		HCV	50%–70%	4–7
N	Population size of IDUs in Australia		215,000	9
P	Total number of no. syringes distributed per year		29,873,802	9
ω	Percentage of syringes distributed that are not used		0.5%–1%	Experimental variable
Behavioral parameters				
m	Average size of a sharing group		2	31,32
p_d	Proportion of IDUs who inject every day		45%–55%	4
f	No. injections per day for IDUs that inject every day		1–2	4
τ	Average no. days between injections for IDUs that inject less frequently than daily		7–21 d	4
n	Average frequency of injecting per IDU per year (weighted average of daily and nondaily injectors)		$n = 365\left[P_d f + (1 - P_d)\frac{1}{\tau}\right]$ (ranges 170–430)	
s	Proportion of IDUs who share syringes		15%–20%	4
q	Proportion of injections that are shared for IDUs that share syringes		13%–17%	4
δ_S	Average no. times each shared syringe is used before disposal		2.6–2.8	4
δ_P	Average no. times each nonshared syringe is used before disposal		Determined by solving equation (2); median 2.1	
Syringe cleaning parameters				
p_c	Proportion of syringes used multiple times by multiple people that are cleaned before reuse		0%–1%	Experimental variable
ε_c	Effectiveness of syringe cleaning	HIV	70%–80%	40,45
		HCV	30%–40%	46–50

injecting post-HCV seroconversion is ~10 years. This is considerably greater than the threshold of 2.3 years required to control HCV incidence. In contrast, the duration of injecting for HIV-infected IDUs postseroconversion is assumed to be much less than for HCV (less than 10 years) and thus less than the critical 11.6 years required to control HIV incidence.

To identify factors that could provide effective targets for intervention, we conducted a sensitivity analysis by means of calculating partial rank correlation coefficients[51] between incidence and the sampled model parameters (results not shown). We determined that the number of times each syringe is used before disposal is the most sensitive behavioral factor in determining the incidence of both HIV and HCV infection followed by the percentage of injections that are shared. Therefore, we investigated the expected change in incidence for HIV and HCV, according to our model, with changes in the frequency of shared injections and the average number of times each syringe is used (Figs. 3A, B). As an example, if the proportion of injections that are shared decreased from 15% to 10%, annual HIV incidence would reduce from 34 cases to 23 and from 10,268 cases of HCV to 6845; that is, a reduction of ~33%. If the average number of times a syringe is shared decreased from 2.7 to 1.5, the annual HIV and HCV incidence would decrease to 19 and 5704 cases, respectively. Obviously, interventions that simultaneously decrease both syringe-sharing frequency and injections per syringe will be even more efficient (Figs. 3A, B).

The number of times each syringe is used can be practically decreased by greater dissemination of sterile

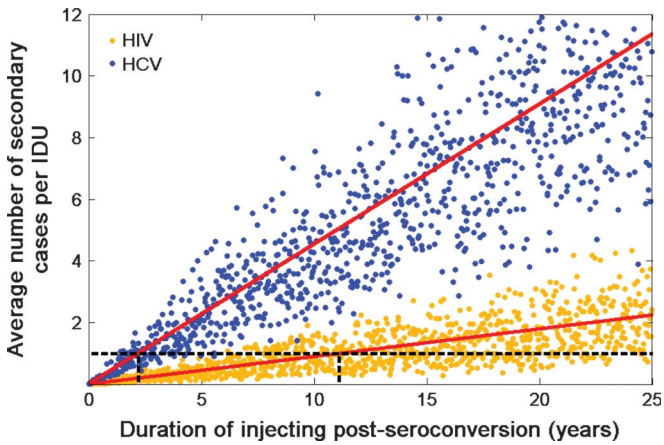

FIGURE 2. The average number of secondary cases of HIV (orange) and HCV (blue) transmission per IDU versus the duration of injecting postseroconversion. The solid lines refer to median simulations and the dashed line refers to one secondary infection.

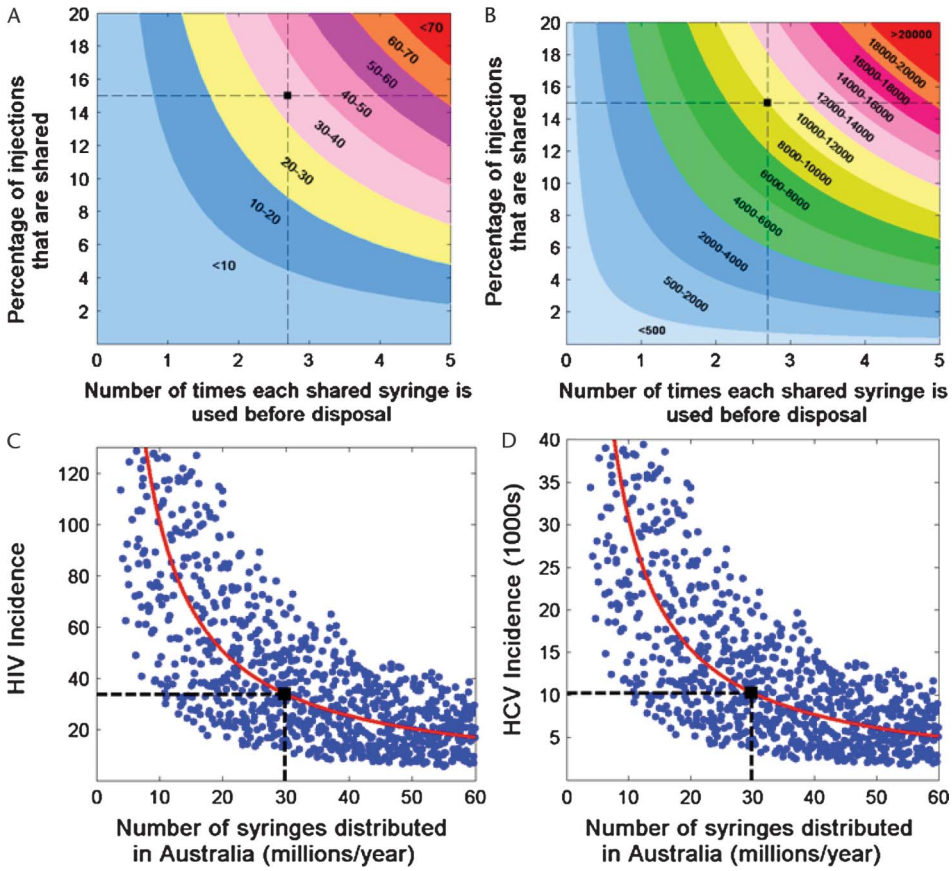

FIGURE 3. The simulated number of annual (A) HIV and (B) HCV transmissions among IDUs in Australia versus the percentage of injections that are shared and the average number of times each syringe is used before disposal. The dashed lines refer to current levels of sharing and syringe use. C and D, scatter plots of the simulated number of annual (C) HIV and (D) HCV transmissions among IDUs in Australia versus the number of sterile syringes distributed in Australia are shown, assuming that syringe distribution changes the average number of times each syringe is used before disposal. The blue dots are results from 1000 simulations, the red curves represent the median parameter values, and the black dashed lines refer to current levels of syringe distribution.

syringes through NSPs. We estimated the expected population-level incidence of HIV and HCV due to changes in syringe distribution levels, under the assumption that changes in supply of syringes alters the average number of times each shared and nonshared syringe is used. In Figures 3C and D, we present the expected change in HIV and HCV incidence due to increases or decreases in the number of syringes distributed. We found a nonlinear association between HIV and HCV incidence and the number of syringes distributed (Figs. 3C, D). Currently, approximately, 30 million syringes are distributed annually through NSPs. We estimate that if distribution was reduced to 10 million syringes, then annual incidence would increase by a factor of ~3, to ~100 and ~31,000 HIV and HCV infections (Figs. 3C, D). A moderate (one third) reduction in the distribution of syringes would increase incidence by ~1.5-fold, to ~51 annual HIV and ~15,000 HCV infections each year (Figs. 3C, D). In contrast, if the number of syringes distributed were doubled, to ~60 million per year, then the expected annual incidence would decrease by ~50% to ~17 HIV infections and ~5100 HCV infections (Figs. 3C, D).

DISCUSSION

Our mathematical model suggests that with current levels of injecting drug use and patterns of risk behavior, the annual distribution of 30 million sterile syringes in Australia has largely controlled HIV transmission among IDUs and that HIV transmission will remain low if current programs remain in place. In contrast, our model illustrates that HCV transmission among IDUs continues to occur at high rates. Furthermore, this model suggests that under most plausible scenarios, several thousand people will continue to be infected with HCV each year.

We found that to sustain an HIV epidemic, the average duration of injecting post-HIV seroconversion is required to be greater than 11.6 years (Fig. 2). It is reasonable to conclude that this threshold is not reached and that HIV incidence among Australian IDUs could be expected to remain low. However, the HCV epidemic will be extremely difficult to eradicate by decreasing the average duration of injecting postseroconversion, which would require reducing this below 2.3 years (Fig. 2). Indeed, our model demonstrates that the 2 epidemics are in completely different phases: HIV infection among IDUs is in a phase of control toward eradication (with the reproduction ratio less than unity), whereas HCV is endemic, and controlling incidence is not possible in the foreseeable future (with the reproduction ratio substantially greater than unity). Therefore, other feasible and effective interventions that reduce HCV incidence are required.

Our analysis suggests that although HCV transmission is unlikely to be eradicated, reductions in the number of times each syringe is used, along with reductions in syringe-sharing frequency, may have a substantial impact on HCV

transmission (Figs. 3A, B). This qualitative result is certainly not new. However, for the first time, we have developed a quantitative relationship between expected incidence and the level of syringe distribution by NSPs. This relationship is of large value to Australian federal and state policy officials and other stakeholders in discussions surrounding the effectiveness of NSPs. Although our model is calibrated to Australian IDU behavior and incidence, the relationship can be used to inform stakeholders in other regions on the likely relative change in incidence due to greater sterile syringe coverage.

Although education and counseling designed to reduce syringe sharing may have a place, increasing syringe coverage through NSPs is likely to be the most effective strategy to reduce incident infections. Increasing syringe coverage aims to decrease the number of times each syringe is shared and reduce the frequency of sharing. Historically, Australia has been able to effectively introduce NSPs and increase the coverage of sterile injecting equipment. There is compelling evidence that NSPs have been effective in preventing HIV infection among IDUs and that Australia has one of the largest and most comprehensive networks of NSPs internationally.[9] Although these achievements should be applauded, greater efforts are required to reduce the transmission of HCV. We suggest that the saturation in demand has not been reached and greater supply would result in greater coverage. It is difficult to estimate the proportion of all IDUs that access NSPs, however, the recent National Drug Strategy Household Survey revealed that only 51% of those who had injected in the last 12 months usually obtained their injecting equipment from public sector NSPs.[55] This indicates that there are opportunities for public sector NSP services to increase client reach. Structural and policy factors also limit access to current NSP services. With the exception of pharmacy-based services, few NSPs operate into the evening or are open on weekends. Although syringe dispensing machines operate 24 hours a day, these are not operational throughout Australia. There are also limits on the quantity and range of syringes freely available at some NSP services. Secondary exchange of sterile needles and syringes (from one IDU to another) is prohibited in most states and territories, and there are some locations where there is demand for NSP but where services are not well developed. These factors suggest that syringe distribution in Australia is limited by supply rather than demand and that increased coverage is possible.

The additional resources required to increase (or double) distribution depend on the methods employed to achieve this aim. Expansion of opening hours and the establishment of new NSP outlets would require significant additional resources, and these measures would most likely be necessary to achieve a doubling of syringe distribution. However, other measures to increase syringe distribution, such as the relaxation of restrictions on the quantity and range of syringes freely available to NSP clients, the removal of impediments to allow secondary exchange by IDU, and the installation of additional syringe vending machines could all be implemented at relatively low cost. In Australia, the costs associated with procurement of needles and syringes are estimated at approximately a quarter of total NSP service budgets. If the above-mentioned low-cost measures were implemented across Australia, a 10% increase in syringe distribution could theoretically be achieved with a modest 2% increase in the total NSP budget.

There are several limitations to our approach. First, our models were based on current levels of injecting drug use. Previous work,[9] and the experience in Australia after a national reduction in heroin supply in late 2000/early 2001, has shown that HCV transmission can be reduced if the number of IDUs can be reduced. We did not consider this in our model, but, if the behavior of IDUs remains constant, greater numbers of people injecting drugs will result in more HIV and HCV transmissions. We used a static model to investigate the expected number of infections in a single year and not how epidemics may evolve over time. A dynamic model would need to consider factors that influence prevalence and the IDU population over time such as mortality, immigration, and cessation of drug injection. Second, our models do not account for HIV or HCV treatment, both of which suppress or eradicate viral replication and could be expected to reduce the risk of transmission. However, rates of HCV treatment uptake by active IDUs are very low in Australia, and the population-level effect on transmission rates can be largely discounted. There is a lack of data on rates of HIV treatment among active IDUs. However, we calibrated our models to current levels of HIV transmission and so our results are broadly applicable as long as current rates of HIV treatment in active IDUs remain stable. Third, our models are based on a number of assumptions. Although we have based our assumptions on available data, these data are based on nonrandom samples or case notifications. Where possible we looked at different prospective observational studies, using different methods and sampling techniques, to obtain robust assumptions. Furthermore, we performed wide-ranging uncertainty analyses, defining ranges of uncertainty around key assumptions, to provide a sense of the robustness of our results. We developed a static model of incidence to explore relationships between key behavioral, biological, and epidemiological parameters and expected annual incidence of HIV and HCV. This model has also been useful to estimate how the expected incidence may change due to changes in syringe distribution through NSPs. Future modeling could investigate how such changes may influence transmission dynamics of epidemics over a longer period. However, as with all mathematical models, assumptions should be reviewed critically and results interpreted cautiously.

Our results support the need for a range of evidence-based public health responses to prevent both primary and secondary HIV and HCV transmission among IDUs. These include biomedical and behavioral prevention interventions which target injecting risk behaviors, interventions designed to encourage early uptake of treatment, and increasing access to HCV treatment. However, although HIV remains low and stable among IDUs in Australia, even relatively minor reductions in current levels of NSP coverage could result in a significant increase in incident infections. The situation is more severe for HCV where the background prevalence is high and increased viral infectivity implies that eradication is unlikely. Although reducing the duration of injecting alone is unlikely to have a significant impact on the current epidemic,

our model suggests that decreasing the number of times each syringe is shared and reducing the frequency of sharing, by doubling NSP coverage, is likely to halve the number of new infections per year. Although our analysis supports the need for a comprehensive HCV prevention strategy, NSPs remain a key component and current gaps in coverage continue to sustain the epidemic. Our results offer strong supportive evidence of the large epidemiological benefits associated with expanding NSP services. This should also include the establishment of NSPs in settings where there is demand and NSP currently does not exist and considering alternative ways of supplying clean injecting equipment such as extending operating hours of NSPs, removing impediments to secondary exchange, and increasing availability of syringe dispensing machines. As we have shown, scaling up the distribution of sterile syringes could result in significant reductions in HCV transmission among IDUs, averting considerable morbidity and mortality and decreasing associated costs.

ACKNOWLEDGMENTS

We acknowledge funding from the Australian Research Council (DP0771620). Lisa Maher is supported by an NHMRC Senior Research Fellowship and David Wilson is supported by an NHMRC Career Development Award. The National Centre in HIV Epidemiology and Clinical Research is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, University of New South Wales.

REFERENCES

1. Wasley A, Alter MJ. Epidemiology of hepatitis C: geographic differences and temporal trends. *Semin Liver Dis*. 2000;20:1–16.
2. WHO, UNAIDS. *AIDS epidemic update: December 2007:* Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO) 2007. Geneva, Switzerland.
3. McDonald A. *Annual Surveillance Report: HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia:* National Centre in HIV Epidemiology and Clinical Research, Sydney, NSW; 2007.
4. Iversen J, Topp L, Maher L. *Australian NSP Survey National Data Report 2002—2006*. National Centre in HIV Epidemiology and Clinical Research, Sydney, NSW: University of New South Wales; 2007.
5. Crofts N, Aitken CK. Incidence of bloodborne virus infection and risk behaviours in a cohort of injecting drug users in Victoria, 1990–1995. *Med J Aust*. 1997;167:17–20.
6. Dore GJ, Law M, MacDonald M, et al. Epidemiology of hepatitis C virus infection in Australia. *J Clin Virol*. 2003;26:171–184.
7. Loxley WM, Phillips M, Carruthers SJ, et al. The Australian Study of HIV and Injecting Drug Use. Part I: prevalence for HIV, hepatitis B and hepatitis C among injecting drug users in four Australian cities. *Drug Alcohol Rev.* 1997;16:207–214.
8. Marsh A, Loxley W, Hawks D, et al. Changes in drug use and HIV/AIDS risk-taking 1989–90. *Drug Alcohol Rev.* 1995;14:201–212.
9. Razali K, Thein HH, Bell J, et al. Modelling the hepatitis C virus epidemic in Australia. *Drug Alcohol Depend*. 2007;91:228–235.
10. Kaldor JM, Archer GT, Buring ML, et al. Risk factors for hepatitis C virus infection in blood donors: a case-control study. *Med J Aust*. 1992;157: 227–230.
11. Strasser SI, Watson KJ, Lee CS, et al. Risk factors and predictors of outcome in an Australian cohort with hepatitis C virus infection. *Med J Aust*. 1995;162:355–358.
12. Roman F, Hawotte K, Struck D, et al. Hepatitis C virus genotypes distribution and transmission risk factors in Luxembourg from 1991 to 2006. *World J Gastroenterol*. 2008;14:1237–1243.
13. Hope V, Ncube F, DeSouza-Thomas L, et al. *Shooting Up. Infections Among Injecting Drug Users in the United Kingdom 2003*. London, United Kingdom: Health Protection Agengy; 2004.
14. D'Cruz OJ, Uckun FM. Clinical development of microbicides for the prevention of HIV infection. *Curr Pharm Des*. 2004;10:315–336.
15. Patz JA, Jodrey D. Occupational health in surgery: risks extend beyond the operating room. *Aust N Z J Surg*. 1995;65:627–629.
16. Kaplan EH, O'Keefe E. Let the needles do the talking! Evaluating the New Haven needle exchange. *Interfaces*. 1993;23:7–26.
17. Hudgens MG, Longini IM Jr, Vanichseni S, et al. Subtype-specific transmission probabilities for human immunodeficiency virus type 1 among injecting drug users in Bangkok, Thailand. *Am J Epidemiol*. 2002; 155:159–168.
18. Henderson DK, Fahey BJ, Willy M, et al. Risk for occupational transmission of human immunodeficiency virus type 1 (HIV-1) associated with clinical exposures. A prospective evaluation. *Ann Intern Med*. 1990; 113:740–746.
19. Cavalcante NJ, Abreu ES, Fernandes ME, et al. Risk of health care professionals acquiring HIV infection in Latin America. *AIDS Care*. 1991;3:311–316.
20. Gerberding JL. Incidence and prevalence of human immunodeficiency virus, hepatitis B virus, hepatitis C virus, and cytomegalovirus among health care personnel at risk for blood exposure: final report from a longitudinal study. *J Infect Dis*. 1994;170:1410–1417.
21. Ippolito G, Puro V, De Carli G. The risk of occupational human immunodeficiency virus infection in health care workers. Italian Multicenter Study. The Italian Study Group on Occupational Risk of HIV infection. *Arch Intern Med*. 1993;153:1451–1458.
22. Nelsing S, Nielsen TL, Nielsen JO. Occupational exposure to human immunodeficiency virus among health care workers in a Danish hospital. *J Infect Dis*. 1994;169:478.
23. Tokars JI, Marcus R, Culver DH, et al. Surveillance of HIV infection and zidovudine use among health care workers after occupational exposure to HIV-infected blood. The CDC Cooperative Needlestick Surveillance Group. *Ann Intern Med*. 1993;118:913–919.
24. Short LJ, Bell DM. Risk of occupational infection with blood-borne pathogens in operating and delivery room settings. *Am J Infect Control*. 1993;21:343–350.
25. Gerberding JL. Management of occupational exposures to blood-borne viruses. *N Engl J Med*. 1995;332:444.
26. MacDonald M, Crofts N, Kaldor J. Transmission of hepatitis C virus: rates, routes, and cofactors. *Epidemiol Rev.* 1996;18:137–148.
27. Kiyosawa K, Sodeyama T, Tanaka E, et al. Hepatitis C in hospital employees with needlestick injuries. *Ann Intern Med*. 1991;115: 367–369.
28. Sodeyama T, Kiyosawa K, Urushihara A, et al. Detection of hepatitis C virus markers and hepatitis C virus genomic-RNA after needlestick accidents. *Arch Intern Med*. 1993;153:1565–1572.
29. Des Jarlais C, Perlis T, Friedman SR, et al. Behavioral risk reduction in a declining HIV epidemic: injection drug users in New York City, 1990–1997. *Am J Public Health*. 2000;90:1112–1116.
30. Donoghoe MC, Stimson GV, Dolan K, et al. Changes in HIV risk behaviour in clients of syringe-exchange schemes in England and Scotland. *AIDS*. 1989;3:267–272.
31. Donoghoe MC, Dolan KA, Stimson GV. Life-style factors and social circumstances of syringe sharing in injecting drug users. *Br J Addict*. 1992;87:993–1003.
32. McKeganey N, Abel M, Taylor A, et al. The preparedness to share injecting equipment: an analysis using vignettes. *Addiction*. 1995;90: 1253–1260.
33. Australian National Council on drugs (ANCD). *Needle and Syringe Programs: position paper*. Canberra: ACT: 2002.
34. *Return on Investment in Needle and Syringe Programs in Australia Report*. Sydney, Australia: Commonwealth Department of Health and Ageing, Health Outcomes International Pvt Ltd, National Centre in HIV Epidemiology and Clinical Research; 2002.
35. Greenhalgh D, Hay G. Mathematical modelling of the spread of HIV/AIDS amongst injecting drug users. *IMA J Math Appl Med Biol*. 1997;14: 11–38.
36. Blower SM, Hartel D, Dowlatabadi H, et al. Drugs, sex and HIV: a mathematical model for New York City. *Philos Trans R Soc Lond B Biol Sci*. 1991;331:171–187.

37. Murray JM, Law MG, Gao Z, et al. The impact of behavioural changes on the prevalence of human immunodeficiency virus and hepatitis C among injecting drug users. *Int J Epidemiol*. 2003;32:708–714.
38. Bacaër N, Abdurahman X, Ye J. Modeling the HIV/AIDS epidemic among injecting drug users and sex workers in Kunming, China. *Bull Math Biol*. 2006;68:525–550.
39. Vickerman P, Hickman M, Rhodes T, et al. Model projections on the required coverage of syringe distribution to prevent HIV epidemics among injecting drug users. *J Acquir Immune Defic Syndr*. 2006;42:355–361.
40. Siegel J, Weinstein M, Fineberg H. Bleach programs for preventing AIDS among i.v. drug users: modeling the impact of HIV prevalence. *Am J Public Health*. 1991;81:1273–1279.
41. Kretzschmar M, Wiessing L. New challenges for mathematical and statistical modeling of HIV and hepatitis C virus in injecting drug users. *AIDS*. 2008;22:1527–1537.
42. Sutton AJ, Gay NJ, Edmunds WJ. Modelling the impact of prison vaccination on hepatitis B transmission within the injecting drug user population of England and Wales. *Vaccine*. 2006;24:2377–2386.
43. Sutton AJ, Gay NJ, Edmunds WJ, et al. Modelling the hepatitis B vaccination programme in prisons. *Epidemiol infect*. 2006;134: 231–242.
44. Sutton AJ, Gay NJ, Edmunds WJ, et al. Modelling the force of infection for hepatitis B and hepatitis C in injecting drug users in England and Wales. *BMC Infect Dis*. 2006;6:93.
45. Abdala N, Gleghorn AA, Carney JM, et al. Can HIV-1-Contaminated Syringes Be Disinfected? Implications for Transmission Among Injection Drug Users. *J Acquire Immune Defic Syndr*. 2001;28:487–494.
46. Hagan H, Thiede H. Does bleach disinfection of syringes help prevent hepatitis C virus transmission. *Epidemiology*. 2003;14:628–629.
47. Agolini G, Russo A, Clementi M. Effect of phenolic and chlorine disinfectants on hepatitis C virus binding and infectivity. *Am J Infect Control*. 1999;27:236–239.
48. Kapadia F, Vlahov D, Des Jarlais DC, et al. Does bleach disinfection of syringes protect against hepatitis C infection among young adult injection drug users? *Epidemiology*. 2002;13:738.
49. *Syringe Disinfection for Injection Drug Users*. Centers for Disease Control and Prevention; 2007. Available at: http://www.cdc.gov/idu/facts/disinfection.htm. Accessed June 2, 2008.
50. Crofts N, Aitken CK, Kaldor JM. The force of numbers: why hepatitis C is spreading among Australian injecting drug users while HIV is not. *Med J Aust*. 1999;170:220–221.
51. Hoare A, Regan DG, Wilson DP. Sampling and sensitivity analyses tools (SaSAT) for computational modelling. *Theor Biol Med Model*. 2008;5:4.
52. National Notifiable Diseases Surveillance System. *Australian Government Department of Health and Ageing (AGDHA)*. Vol 2006. Available at: http://www9.health.gov.au/cda/Source/CDA-index.cfm. Accessed June 12, 2008.
53. Anderson RM, May RM. *Infectious Diseases of Humans: Dynamics and Control*. New York: Oxford University Press; 1991.
54. Maher L, Jalaludin B, Chant KG, et al. Incidence and risk factors for hepatitis C seroconversion in injecting drug users in Australia. *Addiction*. 2006;101:1499–1508.
55. *2007 National Drug Strategy Household Survey: First Results*. Canberra, Australia: Australian Institute of Health and Welfare; 2008.