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Commentary: Modelling and understanding differences in human immunodeficiency and hepatitis C virus epidemiology in injection drug users

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Human immunodeficiency virus (HIV) prevention programmes for injection drug users (IDU) have included elements such as outreach education, testing, counselling, bleach distribution, and wider access to sterile needles through unrestricted pharmacy access and needle exchange programmes. Needle exchange programmes work by providing sterile in exchange for contaminated needles alongside outreach education and health service referrals. With both HIV and hepatitis viruses known to be transmitted by multiperson use of needles and syringes, providing access to sterile needles for those who cannot or will not stop drug use would appear to be an important strategy. An early observational study of the effectiveness of needle exchange programmes showed that harm reduction was associated with reduced rates of hepatitis B and C virus infections,[1] and other observational studies have shown lower rates of HIV.[2,3] However, subsequent work has shown that this is not always the case[4] and that rates of hepatitis C virus (HCV) in IDU have tended to remain elevated even in communities where HIV rates have declined.[5] This discrepancy has been puzzling, and the modelling study by Murray and coworkers in this issue provides a contribution to advance our thinking about this.[6]

Although both HIV and HCV share similarities in that drug users are at risk through parenteral transmission and both are predominantly chronic infections, there are important differences between the two infections. First, the prevalence of infection among drug users is higher for HCV than for HIV, indicating a larger pool of HCV from which transmission can occur. Second, data from needlestick injuries suggest that the rate of transmission per individual needle stick may be about 10 times higher in HCV than HIV infection.[7] Third, indirect sharing and drug preparation practices such as backloading and sharing of the cotton, cooker, and rinse water used to prepare drugs for injection are more frequently associated with transmission of HCV[5,8] than HIV.[9] One report indicating the possibility of transmission with straws used to inhale cocaine suggests an efficiency of transmission for HCV that has not been reported to date for HIV.[10]

Murray *et al.* suggest that these known or suspected epidemiological differences did not fully explain the intriguing situation in Australian injection drug users where the reported HIV prevalence remained very low,[11] but HCV prevalence was about 50% and comparable to that observed in other injection drug user populations with much higher HIV prevalence. To explain this situation they modelled virus transmission among injection drug users via 'classic' needle sharing in such a way as to handle both HCV and HIV while capturing the main differences between the two. An interesting approach was chosen by modelling drug sharing episodes among groups of a given size. The model allowed for calculating critical levels of needle sharing below which total infections would fall to a low prevalence. These levels were estimated to be 17 injection partners per year for HIV and 3 for HCV and were compared to 6 injection partners per year currently estimated in Australia.

Mathematical propagation models such as this have a number of uses. First, they can provide qualitative insights into the relevance of certain key parameters or structural aspects of the dynamics of propagation. The results of this study indicate that behavioural changes in needle sharing starting in the late 1980s in Australia might have been enough to limit the spread of HIV but insufficient to substantially limit or reduce HCV prevalence. Second, modelling may provide the public health community with quantitative predictions of the possible effect of intervention strategies to assist policymaking. Here, the model estimates the number and prevalence of HIV and HCV infections in the injection drug user population of Australia (Figure 2) and the critical level of needle sharing necessary for successfully reducing these infections. The authors should be applauded for having provided estimates of the uncertainty of some of their results, a feature not always included in such modelling studies. However, the uncertainty for HCV prevalence was considerable, with an inter quartile range from 20 to 50% for the year 2000, and these estimates were much more imprecise than those for HIV prevalence (Figure 2). It would have been important to know which of the parameters and their uncertainty was primarily responsible for this substantial difference. No estimates on uncertainty of the critical levels of needle sharing were given, however. These would have enabled better judgement of whether the critical level of three partners per year can indeed be expected to reduce HCV to low levels.

As mathematical modelling studies are inevitably based on assumptions, one can always argue about how appropriate these are, and whether they are unrealistic or too simplistic and therefore hamper firm qualitative or quantitative conclusions about the reality. Here, the authors chose to build the model on

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parameters that reflect the average value over all injection drug users in Australia. For example, the average number of injections per year was chosen to be 60, with a range of 30 to 90. This value was based on cross-sectional data on self-reported needle sharing within the last month and some model-specific equations that allowed this information to be related to the number of injections. Given the heterogeneity in drug consumption intensity between sporadic, regular, and heavily drug dependent injectors, this may be too strong a simplification. More complex compartment modelling would have been necessary to account for that. Additionally, per contact infectivity was assumed to be 2% (0.3–3.3%) for HIV and 4% (1.2–10%) for HCV (Table 1), and constant after infection. However, not all HCV infected individuals remain persistently infected and contact infectivity seems to be higher with higher levels of viral load[12] and can be expected to be much higher in acute viraemia after infection. Incorporating acute viraemia may be necessary to adequately explain the fact that HCV may be transmitted rapidly in the first few years after initiation of injection use, or among very young injectors.[11,13]

In conclusion, the US Public Health Service have issued an HIV Prevention Bulletin[14] to warn injection drug users who could not quit using drugs to use (and then discard) a new sterile needle each time they injected. While rates of HIV have declined, the persistent high rates of HCV and the concern about transmission with even a few partners suggested in this modelling exercise indicate that efforts to encourage single use and discard syringes remain important.

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