Measuring risk of HIV and HCV among injecting drug users in the Russian Federation

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Background: The aim of the study was to measure risk of HIV and HCV infection among injecting drug users (IDUs) through force of infection (FOI) models in three cities of the Russian Federation and assess the value of behavioural data and FOI in predicting risk of infection as a method of second-generation surveillance. Methods: FOI models were fitted to prevalence data collected through an anonymous, cross-sectional community-recruited survey of IDUs with oral fluid sample collection for antibodies to HIV and HCV. Risk of infection was estimated from FOI estimates obtained by fitting a model to prevalence data by length of injecting career for each city and then overall. Risk behaviours were examined by injecting career length. Results: A total of 1473 IDUs were recruited. Prevalence of HIV was 8.1% (95% CI 6.7–9.6%) and HCV 63.4% (95% CI 60.9–65.9%). A higher FOI in new initiates to injecting (injecting career length <1 year) was found for both HIV and HCV compared with experienced IDUs (injecting career length >1 year). Increased risk of infection was not corroborated by injecting risk behaviours amongst new initiates into injecting (n = 38). Only 5.7% (n = 2) reported receptive sharing during the last 4 weeks, 57.9% (n = 22) sharing any injecting paraphernalia, 2.6% (n = 1) frontloading and 8.5% (n = 3) ever injecting with used needles/syringes. However, 29% of new initiates reported exchanging sex in the last 4 weeks (29%) compared with 11% long-term IDUs. Conclusions: FOI models can play an important role in surveillance of HIV but caution is needed in the interpretation of behavioural data for predicting current or future risk of HIV.

Keywords: force of infection, HIV, risk of infection, Russia, surveillance.

Introduction

Evidence points to an HIV epidemic in the Russian Federation contained primarily among injecting drug users (IDUs) that has occurred rapidly with explosive outbreaks at a city level since 1996.¹–⁴ A more recent examination suggests that the total number of HIV case reports registered declined from 88,577 in 2001 to 32,817 in 2004, and the proportion of these reports attributed to injecting drug use has decreased, from 94% to 67% in the same period. HIV case reports have subsequently increased slightly and at the end of 2007 43,997 new cases were registered.⁵ Evidence suggests that HIV case reports generally underestimate the number of HIV cases among IDUs in the Russian Federation since these groups often have poor access or are reluctant to use state-provided services.⁶–⁹ Research among samples of IDUs recruited from non-treatment settings indicate that HIV prevalence remains high,¹⁰,¹¹ particularly among samples of young IDUs suggestive of ongoing recent infection.¹²,¹³

Studies of prevalent HIV infections measure the cumulative incidence of HIV, not recent risk.¹⁴ Recently, it has been argued that the collection of behavioural data can supplement biological data to facilitate the measurement of risk of acquiring HIV and help predict changes in HIV incident rate.¹⁵–¹⁷ Second-generation surveillance guidelines have been developed based on this rationale and use both biological and behavioural data to better understand the factors driving HIV epidemics.¹⁶,¹⁸ There are multiple methodological difficulties in collecting behavioural data among IDUs, particularly when focusing on the measurement of socially undesirable behaviours such as receptive sharing (injecting with a used needle/syringe). Unlike biological indicators where case definitions can be established through laboratory confirmation, measuring risk behaviours relies on respondents’ active participation: refusal, non-response and misreporting can distort results and can lead to an underestimation or overestimation of risk.¹⁷,¹⁹–²²

Measuring incidence of HIV within a population may provide a more accurate measure of current risk behaviours. A measure of incidence can be estimated from cross-sectional surveys or surveillance data by estimating the force of infection (FOI).²³,²⁴ The FOI is the estimate of per capita rate at which susceptible (i.e. seronegative) IDUs acquire infection. It may be produced by fitting a model to prevalence data by period of risk, where the prevalence quantifies the proportion of individuals antibody positive.²⁵,²⁶

Guidelines of the World Health Organization and United Nations agencies¹⁶,²² recommend second-generation surveillance approaches using both biological and behavioural data to better understand factors driving the epidemic among young populations engaging in high risk behaviours. In keeping with such approaches, we measured the risk of HIV and HCV infection through FOI models in a cross-sectional community survey of IDUs in Moscow, Volgograd and Barnaul in the Russian Federation. FOI estimates were also compared alongside key behavioural data on risk to assess the
Methods

We conducted a cross-sectional survey of 1473 IDUs recruited from non-treatment settings in three cities of the Russian Federation: Moscow (n = 454); Volgograd (n = 517); and Barnaul (n = 501). A detailed description of the survey methods is described elsewhere. In brief, recruitment took place from non-treatment settings through indigenous field workers with expert knowledge of the drug injecting scene in each city, who recruited participants via snowball sampling through injecting networks. Multi-site and multi-network recruitment was used in order to increase the diversity of the sample as much as possible. To be eligible for the study, participants had injected drugs in the previous 4 weeks and consented to provide oral fluid samples for testing for anti-HIV, anti-HCV and Treponema pallidum. The test for T. pallidum detected both current and past infections. All participants completed an interviewer-administered questionnaire containing questions on demographic characteristics, injecting, sexual risk behaviours, contact with health services and history of drug treatment, prison and police contact. Biological and behavioural data were collected anonymously and unlinked to individuals.

Calculating the force of infection for anti-HIV and anti-HCV

Assuming that individuals are seronegative prior to the commencement of their injecting career the FOI was estimated by fitting a model to prevalence data by injecting career length, initially separately for each of the three cities and then for all the data.

It was considered that the FOI may vary with injecting career length where this is calculated throughout this analysis as the difference between the age at the time of survey and the age at the time of the first injection. The model was fitted to data using maximum likelihood to minimise the deviance. A detailed description of the statistical methods used is attached in Appendix 1.

Due to paucity of data and recall issues for individuals with longer injecting career lengths, this analysis has been restricted to participants reporting injecting for ≤5 years. Starting with the full model and taking a piece-wise constant value for each FOI parameter by injecting career length, nested models were compared using the analysis of deviance with the $\chi^2$-test, the criteria for dropping parameters being $P > 0.05$. When selecting the nested models parameters were grouped so the FOI for IDUs with shorter injecting careers are in smaller groups than longer term IDUs to reflect the more consistent injecting behaviour of older initiates. When the parsimonious model (the best-fitting model with the fewest parameters) had been identified, confidence intervals were calculated using profile likelihood.

Examining assumptions underpinning FOI estimates

The FOI analysis used here is based on three assumptions: (i) the risk of infection has not changed over the previous 5 years (the maximum injecting career length of those included in the data); (ii) IDUs were at risk of infection throughout the whole of their injecting career; and (iii) there was no infection prior to initiation of injecting.

The behavioural data were examined to assess whether these assumptions underlying the FOI analysis are reasonable.

The constancy of exposure over time was assessed by examining injectors’ reports of number of attempts at stopping injecting and duration of cessation. Pre-existing infection with HIV prior to initiation into injection was assessed through injectors’ self-reported HIV status and history of HIV testing. The gender distribution of the sample and prevalence of antibodies to T. pallidum was examined as indicators of prior sexual transmission.

Comparing FOI estimates with behavioural data

Key demographic, environmental and injecting risk behaviours were compared by duration of injection, defined by the FOI model, using Pearson’s $\chi^2$-test for categorical variables or t-test with equal variance for continuous variables. The purpose of this analysis was to assess whether the behavioural data suggested significant differences in risk between recent and longer term injectors and whether these differences were corroborated by the FOI analysis.

Results

Overall, 1473 injection drug users were recruited, of whom 29.5% (n = 433) were women. A total of 698 reported injecting for ≤5 years (47.5%). Across the sites 18 IDUs refused to take part in the survey when approached.

Figure 1 shows data on the prevalence of HCV and HIV from all three cities with variation in the injecting career length and the fit of the most parsimonious model for each infection to these data. There was very little difference in the FOI estimates when comparing data from each city (results not shown) and therefore only results estimated from the whole sample are shown. The FOI estimates for HCV were 0.55 (95% CI 0.42–0.70) for new initiates (injecting for <1 year) and 0.13 (95% CI 0.07–0.20) for longer term IDUs (between 1 and 5 years) (figure 2). While for HIV the FOI estimates were 0.07 (95% CI 0.05–0.10) for new initiates and 0 (95% CI 0.0–0.01) for longer term injectors. Considering the FOI results a total of 38 (2.5%) respondents reported that they had been injecting for ≤1 year and a total of 660 (47.5%) reported injecting between 1 and 5 years (longer term injectors).

The result of the model fitting procedure for each infection is shown in table 1. For HCV when the fourth duration of injecting band was dropped, it was found that the extra parameter describing this was statistically significant ($P = 0.007$) and therefore this was included. For the HIV model, the presence of the extra parameter describing injecting career lengths >1 year was found to be statistically significant ($P < 0.0001$) and this was included.

Constancy of exposure

Among IDUs injecting for ≤5 years, 57% reported stopping injecting for a time, the median number of times this occurred was once and the median duration of time stopping was 21 days (data not shown).

Evidence of pre-existing infection

The majority of the sample reported having an HIV test (76.9%, n = 528), and 61.3% reported being tested within the last year prior to the survey (n = 421). Only 1.9% reported themselves HIV positive (n = 13). Among recent initiates into injecting 57% (n = 21) reported having an HIV test in the last year and no-one reported themselves to be positive. A total of 30 (78%) of the new initiates are female, far higher than the overall proportion of female IDUs in the rest of the sample (30%, $P < 0.001$). The prevalence of antibodies to T. pallidum was the same at ~11% in both groups ($P = 0.91$) (table 1).
Injecting risk behaviours by duration of injection

Table 2 summarises sample characteristics by duration of injection. In accordance with the FOI results, characteristics and risk behaviours were compared between new initiates and longer term injectors. Proportionally more new injectors were female ($P = 0.001$), and reported exchanging sex for money, drugs or goods in the last 4 weeks ($P = 0.001$). New injectors were on average younger (19 years) compared with the rest of the sample (24.5 years, $P < 0.001$). Regarding injecting risk behaviours, recent initiates into injecting were less likely to report ever having shared a needle/syringe than longer term injectors ($P < 0.001$) or having engaged in this behaviour in the last 4 weeks ($P < 0.03$). There was no difference in the proportions reporting frontloading (the process by which a drug solute is squirted from a donor syringe by removing the needle) between the two groups ($P = 0.54$), or use of any communal paraphernalia (filters, spoons, or injecting with pre-filled syringes) in the last 4 weeks ($P = 0.75$). Approximately half the sample reported that their sex partner was also an IDU and this did not differ by duration of injection ($P = 0.82$).

Proportionally more longer term injectors reported ever having been tested for HIV compared with recent initiates ($P = 0.04$), but there was no difference in self-reported HIV status, with the overwhelming majority reporting themselves negative ($P = 0.38$). Similarly, proportionally more longer term IDUs reported a history of HCV testing than recent initiates ($P < 0.001$). All recent initiates reported themselves HCV negative compared with only 61.1% of longer term IDUs ($P < 0.001$). No recent initiates reported ever receiving treatment to modify their drug use, just under a quarter of longer term injectors reported a history of drug treatment ($P = 0.001$). There was no difference in prevalence of HIV ($P = 0.72$), HCV (0.25) or $T. pallidum$ (0.61).

Discussion

The FOI models point to a high risk of HIV and HCV infection among recent initiates into injecting in Moscow, Volgograd and Barnaul, highlighting the vulnerability of new injectors to infection. The behavioural data suggest that new injectors are engaging in less risky injecting behaviours, but proportionally more reported exchanging sex in the last 4 weeks.

The extent to which the assumptions underpinning the FOI analysis are upheld is crucial to the interpretation of the findings. In terms of constancy of exposure, the patterns of cessation and abstinence from drug use reported here is comparable to other studies and suggest that IDUs have had continuous exposure to injecting related risks during their injecting career. Evidence suggests that the pattern of drug use changed between 1998 and 2003, with a move from...
injection of home-made opiates to heroin use characterised by more individualised consumption and this may alter risk of infection.\textsuperscript{31} Other evidence suggests that the practice of group injection that prevailed through the communal preparation and use of home made drugs has carried on across the transition to heroin injection.\textsuperscript{32}

Without serial data it is difficult to determine whether the risk of HIV infection among our sample has remained constant over the 5-year period prior to the implementation of the survey (1998 and 2003). Some previous data from Moscow suggests the level of HIV transmission has remained constant with prevalence of 5\% reported in 1998\textsuperscript{33,34} and 8\% in our survey in 2003. Other research shows that HIV transmission among IDUs varies by city and has remained high over the period\textsuperscript{12,13}. Prevalence of HCV has remained consistently high among IDUs nationally, though there is little data on incidence.

The assumption of no HIV/HCV infection prior to exposure is supported by the lack of self-reported HIV status among new initiates despite high levels of HIV testing in the past year. The validity of this self-reported data is hard to determine. These may be incident infections, but some are likely to be misclassified with respondents under-reporting their positive status. The prevalence of antibodies to \textit{T. pallidum} was no higher among new initiates than in the rest of the sample suggesting that this infection is likely to be historical and HIV case reports from the three cities suggest the population prevalence of HIV to be low at <1\% in each city limiting the likelihood of sexual transmission occurring prior to initiation into injecting.

The higher proportion of female IDUs among new initiates and female IDUs with a recent history of sex work points to an increased possibility of sexual transmission of HIV among this subsample and may explain the increased risk of infection for the new initiates seen here. Sex work has been found to be associated with HIV seroconversion in other IDU studies.\textsuperscript{35,36}

Several other factors could explain the higher risk of HCV and HIV among new initiates. One explanation could be changes in incidence or a recent outbreak, although this would result in an increase in the FOI across all injecting career lengths. Another explanation is that selection bias or heterogeneity in the sample causes a core group of IDUs to be infected first. The implementation of repeat surveys over time are needed to understand whether the high FOI is an indication of increasing incidence and prevalence, an outbreak or a product of sampling bias or a core group effect.

The discrepancy between the biological and behavioural data underlines the limitations of using behavioural data to facilitate the measurement of risk of acquiring HIV/HCV and predicting changes in HIV/HCV incident rates. The low prevalence of reported injecting risk behaviours and lack of association with injecting used needles/syringes and HIV or HCV may be due to underreporting and occur inadvertently during drug preparation, or it may be due to an inappropriate time frame used in the analyses with seroconversion occurring prior to the 4-week period.\textsuperscript{30–42} HIV infection is also dependent on multiple factors including: contact patterns within the population; size of the population at risk and

<table>
<thead>
<tr>
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<th>New injectors</th>
<th>Longer term injectors</th>
<th>$\chi^2$ or $t$-test</th>
<th>$P$-value*</th>
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<tr>
<td></td>
<td>$n$</td>
<td>Percentage or mean (SD)</td>
<td>$n$</td>
<td>Percentage or mean (SD)</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>19.1 (2.5)</td>
<td>1351</td>
<td>24.5 (4.5)</td>
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<tr>
<td>Demographic indicators</td>
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<td></td>
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<tr>
<td>Age</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>21.1</td>
<td>361</td>
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</tr>
<tr>
<td>Female</td>
<td>30</td>
<td>78.9</td>
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<td>Injecting risk behaviours</td>
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<td>Ever injected with used needle-syringe?</td>
<td>3</td>
<td>35</td>
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<tr>
<td>Injecting risk behaviours in last 4 weeks</td>
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<td>Frontloaded?</td>
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<td>2.6</td>
<td>88</td>
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<td>Use of any communal paraphernalia (filters, spoons, injecting with pre-filled syringes)?</td>
<td>34</td>
<td>89.5</td>
<td>1142</td>
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<td>Sexual risk behaviours</td>
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<td>Exchanged sex for money, drugs or goods in the last four weeks? (Females only)</td>
<td>11</td>
<td>28.9</td>
<td>72</td>
<td>10.9</td>
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<td>IDU sex partner in last 12 months</td>
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<td>47.2</td>
<td>676</td>
<td>52.6</td>
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<td>Environmental indicators</td>
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<td></td>
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<tr>
<td>History of HIV testing?</td>
<td>23</td>
<td>62.2</td>
<td>1103</td>
<td>82.7</td>
</tr>
<tr>
<td>Self-reported as HIV negative at last test</td>
<td>37</td>
<td>100.0</td>
<td>1284</td>
<td>96.3</td>
</tr>
<tr>
<td>History of HCV testing?</td>
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<td>43.2</td>
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<td>75.3</td>
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<td>Received treatment for drug use?</td>
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<tr>
<td>HIV</td>
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<td>107</td>
<td>8.5</td>
</tr>
<tr>
<td>HCV</td>
<td>16</td>
<td>43.2</td>
<td>818</td>
<td>63.1</td>
</tr>
<tr>
<td>\textit{T. pallidum}</td>
<td>4</td>
<td>11.1</td>
<td>148</td>
<td>11.7</td>
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</table>

*Derived from Pearson $\chi^2$- or $t$-test with equal variance for continuous variable
population prevalence as well as size and composition of sharing networks which cannot be detected in this analysis.

Limitations

There is some chance that the high FOI estimate for new injectors could have been partly due to misclassification, with IDUs underestimating the amount of time they had been injecting. The analysis is based on a very small sample of new injectors, of which 10% tested positive therefore potentially introducing bias into results. The unusual gender structure of the sample suggests the influence of a core group effect and reduces the ability to apply these findings to other city contexts. The FOI estimates are also based on cross-sectional data estimated from the current prevalence which cannot consider differential mortality by HIV status over injecting career length. This is a limitation and particularly pertinent in a setting with poor access to HAART for IDUs. There is also evidence to suggest that HCV antibody responses decrease over time and so could partly explain a lower FOI in older injectors. However, limiting the analysis to IDUs injecting for ≤5 years is likely to have reduced the effect of these issues. The same analysis was repeated on the whole sample and produced similar FOI results (data not shown).

Conclusions

Despite observed decreases in HIV case reports associated with IDUs, our findings suggest that the risk of HCV and HIV among IDUs remains high among non-treatment samples of IDUs and suggests that sex work may be playing a role in increasing the risk of HIV among IDUs. HIV/HCV interventions in the Russian Federation should be sustained and scaled up, particularly targeting recent initiates into injecting to prevent new infections. Findings suggest a potential role for FOI modelling alongside behavioural surveillance in second-generation surveillance for highlighting specific population groups in need of early interventions. FOI modelling on second-generation surveillance studies such as this may provide a lower cost method for providing estimates of the immediate risks of HIV/HCV infection among populations of IDUs. Considering the limitations of the methods employed and the uncertainties in the assumptions, the findings presented should be viewed as exploratory. Further research is needed to corroborate out findings such as the use of detuned assay to confirm incident infections are recent, using a larger sample of new initiates, or comparing with other models to assess FOI combined with sensitivity analyses. However, the lack of agreement between the behavioural data and FOI estimates suggest caution should be taken in the interpretation of behavioural data for predicting current or future risk of HIV/HCV and methods to improve measures of injecting risk behaviours should be explored in order to improve surveillance of behavioural data for second-generation surveillance.

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Conflicts of interest: None declared.

Key points

- Despite observed decreases in HIV case reports associated with injecting drug use in the Russian Federation, our findings suggest that the risk of HCV and HIV among IDUs remains high among non-treatment samples of IDUs and suggests that sex work may be playing a role in increasing the risk of HIV among IDUs.
- Findings suggest a role for FOI modelling alongside behavioural surveillance in second-generation surveillance for highlighting specific population groups in need of early interventions.
- Our findings reinforce the need to employ both sexual and biological data to detect and monitor trends in HIV for second-generation surveillance and highlight the limitations of inferring risk of HCV and HIV among IDUs from behavioural data alone.

References

Appendix 1

It was considered that the FOI (\(\lambda\)) may vary with injecting career length (\(\tau\)) where this is calculated throughout this analysis as the difference between the age at the time of survey and the age at the time of the first injection. The prevalence \(P(\tau)\) quantifies the expected proportion of individuals antibody positive with injecting career length \(\tau\). Prevalence for those who have injected for \(\tau\) years is:

\[
P(\tau) = 1 - e^{-\Lambda(\tau)}
\]

where \(\Lambda(\tau)\) is the cumulative force of infection for those who have injected for \(\tau\) years and is given by:

\[
\Lambda(\tau) = \int_0^\tau \lambda(t) dt
\]

The model was fitted to data using maximum likelihood to minimise the deviance. As the data are binomial the saturated likelihood and model likelihood are:

\[
L^* = \sum_i\left( a_i \ln(P_i) + b_i \ln(1 - P_i) \right)
\]

\[
L = \sum_i\left( a_i \ln(M_i) + b_i \ln(1 - M_i) \right)
\]

where \(a_i\) and \(b_i\) is the observed number of positives (data) and negative with injecting career length \(i\) respectively

\[
p_i = \frac{a_i}{a_i + b_i}
\]

\(M_i\) is the modelled proportion positive with injecting career length \(i\)

**The deviance is:**

\[
D = 2(L^* - L)
\]

Due to paucity of data and recall issues for individuals with longer injecting career lengths, this analysis has been restricted to participants reporting injecting for \(\leq 5\) years. Starting with the full model and taking a piece-wise constant value for each FOI parameter by injecting career length, nested models were compared using the analysis of deviance with the \(X^2\)-test, the criteria for dropping parameters being \(P > 0.05\). When selecting the nested models parameters were grouped so the FOI for IDUs with shorter injecting careers are in smaller groups than longer term IDUs to reflect the more consistent injecting behaviour of older initiates. When the parsimonious model (the best-fitting model with the fewest parameters) had been identified, confidence intervals were calculated using profile likelihood.26

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