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Modelling HIV in the injecting drug user population and the male homosexual population in a developed country context

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ABSTRACT

In many high income countries men who have sex with men (MSM) and injecting drug users (IDUs) are the two groups with the highest HIV prevalence. Yet these two groups are not mutually exclusive, and those MSM who are also IDUs (MSM–IDUs) may be particularly vulnerable to HIV infection. This may be particularly relevant to the IDU population in countries, like the UK, with a much lower HIV prevalence amongst IDUs than MSM, as the MSM–IDUs could provide a route of HIV infection into the IDU population.

In this research two alternative modelling approaches that describe the transmission dynamics of HIV within the IDU, MSM, and heterosexual populations are proposed. These models are constructed with two aims. The first is to investigate the possible impact of interventions that target HIV transmission in the MSM and IDU populations, and the second aim is to investigate the impact of the model structure on the model results. An examination of the assortativity of mixing between risk groups is also undertaken. The models are parameterised for England and Wales.

While the MSM–IDU population is small, targeting MSM–IDUs was the most efficient intervention strategy in terms of cases averted per 100 individuals targeted with the intervention. Sensitivity analysis showed that variations in the assumed assortativity of mixing between the population groups in both models have a large impact on model results. This means that to generate quantitatively robust estimates for the impact of different intervention strategies it will be necessary to obtain estimates for assortativity values through empirical work.

Introduction

Injecting drug users (IDUs) are at increased risk of HIV infection due to their at-risk behaviour. This may be due to the sharing of syringes and other injecting paraphernalia (Hope et al., 2002), but a risk from sexual transmission may also be present (Noone et al., 1993; Strathdee and Stockman, 2010). Sexual risk may be particularly relevant given the number of (particularly female) sex workers that may also be IDUs.

In many high income countries men who have sex with men (MSM) and IDUs are the two groups with the highest HIV prevalence (van de Laar and Likatavicius, 2009). Yet these two groups are not mutually exclusive, and those MSM who are also IDUs (MSM–IDUs) may be particularly vulnerable to HIV infection. This may be particularly relevant to the IDU population in countries, like the UK, with a much lower HIV prevalence amongst IDUs than MSM, as the MSM–IDUs could provide a route of HIV infection into the IDU population.

Previous studies have investigated the assortativity of mixing between different risk groups that may lead to HIV infection being transmitted more or less rapidly between risk groups. Two such examples are the studies by Garnett and Anderson (1993) and Grassly et al. (2003). The study by Garnett and Anderson (1993) examined the impact of heterosexual mixing on HIV prevalence stratifying sexual risk behaviour based on different ages and sexual classes (further stratified on the basis of rates of sexual partner change) while meeting constraints of balancing the

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supply and demand of sexual partners. The authors concluded that the pattern of mixing between age and sexual activity classes, combined with the assumptions made to balance supply and demand between the sexes has a major influence on the predicted pattern of HIV spread and the demographic impact of AIDS. Grassly et al. (2003) investigated HIV infection due to injecting drug use and sexual transmission in the Russian Federation, China and India. The authors proposed a model that described HIV transmission with risk groups being stratified based on their varying sexual and injecting at-risk behaviour. However homosexual behaviour was not considered in their model. The authors concluded that in the emerging HIV epidemics in Russia, India and China unsafe sex played a central role in driving HIV prevalence.

The objective of this study is to investigate through use of two simple models how targeted interventions may impact on the prevalence of HIV. Of particular interest will be the MSM–IDU population and how targeting this relatively small population may impact on the HIV prevalence in the much larger IDU, MSM, and general populations using a low prevalence setting, in this case England and Wales as the focus of this study. Each of the studies described above has shown the potential importance of mixing between risk groups in the epidemiology of HIV, and so in this study an examination of the assortativity of mixing between risk groups will also be undertaken to examine how this may impact on the key results obtained from the model. The model will be parameterised through the use of unlinked anonymous surveys from England and Wales (Health Protection Agency, 2010), and where this data is not sufficient additional secondary data sources will be used.

Methods

We start by defining a general model framework, within which we define the two epidemic models used in this study. These models will be used to investigate both the impact of assortativity and the impact of targeting alternative population sub-groups (which are assumed throughout this study to be disjunct) particularly the MSM, IDU, and MSM–IDU populations (which have higher HIV prevalences) with interventions to reduce the number of cases of HIV in an England and Wales setting. Additionally the impact of increased model complexity on model results will also be investigated.

Model structure

In this study, the focus is on using data describing the overall prevalence of HIV by qualitative risk behaviour rather than considering different HIV disease states and levels of risky activity, so we consider a relatively simple model compared to existing approaches (Grassly et al., 2003).

The general model

Our general model is stratified by disease state, with individuals either susceptible (S) or infected (I); by injecting behaviour i, which is 0 for individuals that do not inject drugs and 1 for IDUs; and by sexual behaviour r. In the general model below different values of r are not explicitly defined, however in Model One below, r stands for either 'non-MSM' or 'MSM'; and in Model Two below r stands for 'male heterosexual', 'female', or 'MSM'. We therefore write $N_r^i = S_r^i + i_r^i$ for the number of individuals in the population with injecting behaviour i and sexual behaviour r, with each individual either susceptible or infectious. The population dynamics are then given by:

$$\begin{aligned}
\frac{dS_r^0}{dt} &= \Phi_r^0 - [\Lambda_r^0(t) + \mu]S_r^0(t) + \tilde{\mu}S_r^1(t)\\
\frac{dI_r^0}{dt} &= \Lambda_r^0(t)S_r^0(t) - \mu I_r^0(t) + \tilde{\mu}I_r^1(t)\\
\frac{dS_r^1}{dt} &= \Phi_r^1 - \Lambda_r^1(t)S_r^1(t) - [\mu + \tilde{\mu}]S_r^1(t)\\
\frac{dI_r^1}{dt} &= \Lambda_r^1(t)S_r^1(t) - [\mu + \tilde{\mu}]I_r^1(t)
\end{aligned} \tag{1}$$

Φ_r^i is the rate at which individuals with injecting behaviour i and sexual behaviour r are recruited into the population, and $\Lambda_r^i(t)$ is the force of infection experienced by such individuals at time t (which is determined by the number of infectious individuals in the population of different types at that time). As data used in this study is from those aged 15–49 years, it is assumed that all individuals leave the population at constant rate $\mu = (1/35)\,\text{years}^{-1}$ and similarly IDUs cease injecting at constant rate $\tilde{\mu} = (1/10)\,\text{years}^{-1}$. Throughout this study, death from HIV has not been considered as the majority of HIV deaths are likely to occur outside the age range considered (Smith et al., 2010), although this possibility could be added to the model.

Parameterisation of model from data

We assume that in a developed country context, several decades after the emergence of HIV, the infection dynamics (1) are at equilibrium. This means that

$$\begin{aligned}
\Phi_r^0 &= \mu N_r^0 - \tilde{\mu}N_r^1\\
\Phi_r^1 &= (\mu + \tilde{\mu})N_r^1\\
\Lambda_r^0 &= \frac{\mu I_r^0 - \tilde{\mu}I_r^1}{N_r^0 - I_r^0}\\
\Lambda_r^1 &= \frac{(\mu + \tilde{\mu})I_r^1}{N_r^1 - I_r^1}
\end{aligned} \tag{2}$$

We then substitute in data for N and I to give Φ_r and the force of infection acting on individuals in each risk group. The full details of this fitting method are given in Electronic supplementary material (ESM).

Model One

In this model the mixing between population groups (heterosexual non-IDU, heterosexual IDU, MSM, MSM–IDU) is simplified so that the impact of assortativity on model results can be more clearly investigated (see Fig. 1, left hand side). This model assumes proportionate mixing plus additional within-group assortative mixing. This arises when individuals make contact in a manner that may lead to infection (either injecting or sexual) with other people in their own or other sub-groups in proportion to the number of contacts that are supplied from each sub-group (Diekmann and Heesterbeek, 2000; Sutton et al., 2006). Two factors are introduced to parameterise the force of infection: a vector of relative risk, whose values represent the propensity of each group to engage in risky behaviour, ρ_r^i; and an assortativity parameter α taking a value of 0 for complete random mixing and 1 for mixing that only

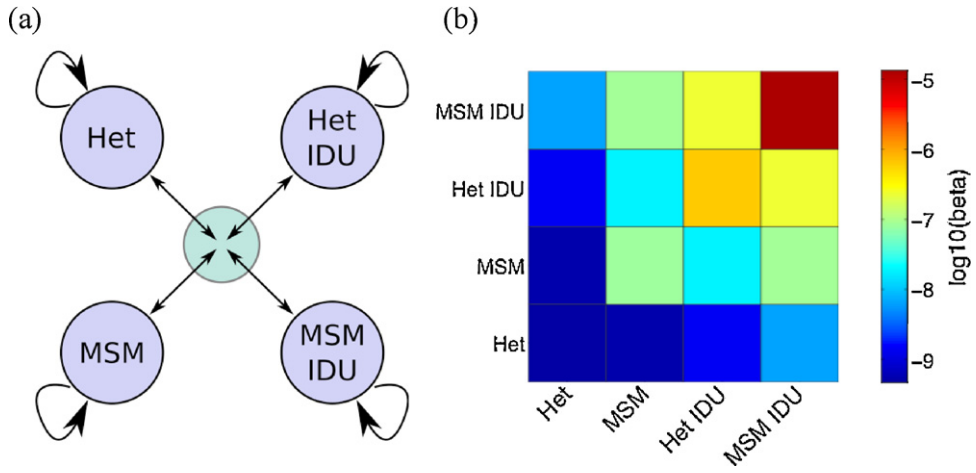

Fig. 1. (a) The risk groups and transmission routes for Model One. The routes enhanced by assortativity are shown with large arrows. In Model One, risk classes interact preferentially with themselves, and contribute to (and experience infection from) a general pool of infection outside the risk group. (b) The mixing matrix for baseline parameters.

occurs within the group. The force of infection is then taken to be a similar form to that used in Garnett and Anderson (1993):

$$\Lambda_r^i = \lambda \rho_r^i \left(\alpha \rho_r^i I_r^i + (1-\alpha) \sum_{q,j} \rho_q^j I_q^i \right)$$

where λ is a scaling factor and r and q can stand for 'non-MSM' or 'MSM' respectively. In this model, we introduce a scaling convention for ρ to give as many unknown parameters as knowns:

$$I = \sum_{r,i} \rho_r^i I_r^i$$

In the absence of assortativity ($\alpha = 0$) there is an analytic solution to the equilibrium equations (2) above, while for $\alpha > 0$ Eq. (2) can be solved numerically, in this case using the MATLAB function `fzero()`. We can then find model parameters (ρ_r^i, λ) that reproduce known population demographics and HIV prevalence prior to the implementation of any interventions.

Model Two

A failing of the previous model is that given it only has one parameter describing mixing between population groups; this makes it difficult to realistically include gender in the model. For example heterosexual males that do not inject do not exhibit mixing behaviour amongst themselves that will lead to the transmission of HIV, whereas males that do inject will. Therefore our second model takes forward Model One and partitions the non-MSM population into males and females (see Fig. 2 left hand side). This means that a more complex form describing mixing becomes necessary, based on retaining Eqs. (1) and (2) above, but using the sexual mixing matrix

$$\beta^{\text{sex}} = \begin{bmatrix} 0 & \beta_{\text{Het}} & 0 \\ \beta_{\text{Het}} & 0 & \beta_{\text{MF}} \\ 0 & \beta_{\text{MF}} & \beta_{\text{MSM}} \end{bmatrix}$$

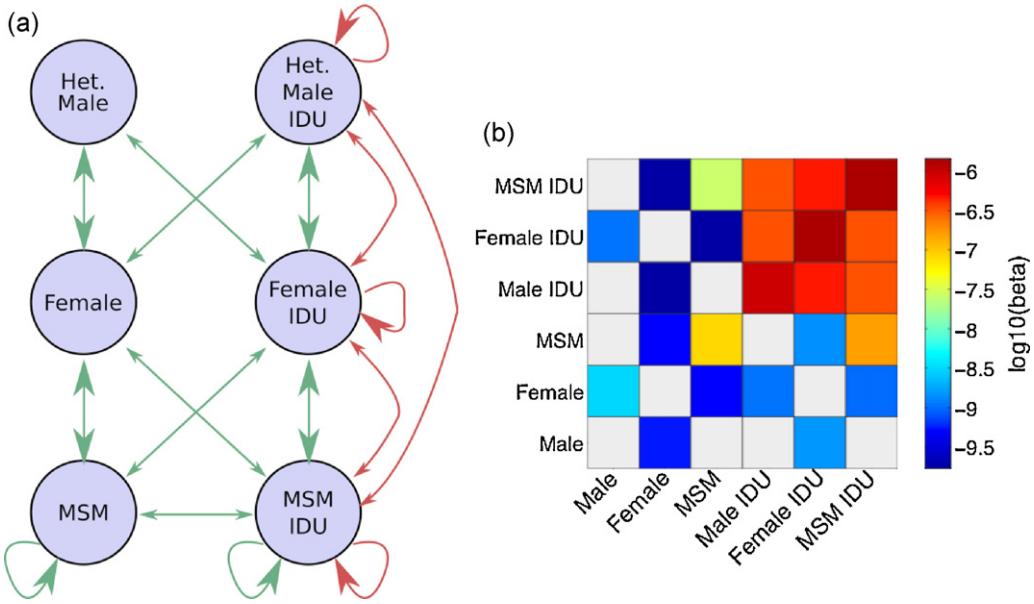

Fig. 2. (a) The risk groups and transmission routes for Model Two. The routes enhanced by assortativity are shown with large arrows. Sexual transmission (shown in green) and injecting transmission (shown in red) are differentiated. (b) The mixing matrix for baseline parameters. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

This matrix incorporates sexual mixing between heterosexual males and females, β_{Het}; sexual mixing between males β_{MSM}; and sexual mixing between females and MSM β_{MF}. The force of infection for non-IDUs is

$$\Lambda_r^0 = \sigma_r^0 \sum_a \beta_{rq}^{\text{sex}} (\alpha_1 I_q^0 \tau_q^0 + (1-\alpha_1) I_q^1 \tau_q^1)$$

where $0.5 < \alpha_1 < 1.0$ is an assortativity parameter, which is higher if individuals have more of a propensity to mix sexually with individuals of the same injecting status. Values of assortativity below 0.5 are possible, but represent disassortative mixing in which individuals of differing injecting status have a greater tendency to mix sexually. We consider this to be unrealistic. In contrast to Model One, here r and q can stand for 'male heterosexual', 'female' or 'MSM'. The other significant difference between this model and Model One is that in place of a vector of relative risk ρ, we find that obtaining an accurate fit to data leads us to introduce distinct vectors of susceptibility σ and transmissibility τ to fit to data and model relevant interventions. The force of infection on IDUs is similar, but needs to include transmission through injecting:

$$\Lambda_r^1 = \left[\sum_q \beta_{rq}^{\text{sex}} (\alpha_1 I_q^1 \tau_q^1 + (1-\alpha_1) I_q^0 \tau_q^0) \right] + \beta_{\text{IDU}} \left[\alpha_2 I_r^1 \tau_r^1 + (1-\alpha_2) \sum_{q \neq r} I_q^1 \tau_q^1 \right]$$

where $0.5 < \alpha_1 < 1.0$ and $0.5 < \alpha_2 < 1.0$ are the assortativity parameters, which in the case of α_2 is higher if individuals have more of a propensity to inject with individuals of the same gender/sexual activity, while as before α_1 is higher if individuals are more likely to have sexual contact with individuals of the same gender/injecting activity class. Again, values below 0.5 are conceptually possible, but unrealistic for the population under consideration.

The rates β_{Het}, β_{MF}, β_{MSM}, β_{IDU} can be found in an analytically closed form for the steady state in terms of other parameters, and this is shown in the ESM. Our methodology is then to specify the two assortativity parameters, and to fit the susceptibility vector σ numerically using the MATLAB function `fmincon()`. We were able to obtain good fits even if the baseline transmissibility vector τ was always unity, and so we made this assumption to reduce the number of model parameters. The susceptibilities of exclusively heterosexual males (IDU and non-IDU), and of the IDU–MSM population, are taken to be unity since the β rates above can be rescaled to accommodate this choice without changing model predictions, leaving this as a three-dimensional constrained non-linear optimisation problem. Details of the optimisation method used are provided in ESM.

Implementation of interventions

The purpose of investigating the hypothetical interventions in this study is to show how targeting specific sub-populations can impact on the spread of HIV transmission within the wider population. And while the interventions used in this study are hypothetical, they will provide an insight into which sub-populations can be targeted to maximise the reduction in the number of new HIV cases, as well as showing which interventions are likely to be most efficient in terms of number of HIV cases averted as a proportion of the size of the sub-population targeted.

Interventions are implemented in Model One by changing the proportion of a specific at risk population that is no longer susceptible to infection from HIV. This of course means eliminating the at-risk behaviour that may lead to the transmission of HIV, which might include reduction in sex workers, injectors that share, or reducing the contact with infected individuals.

We model interventions designed to target the behaviour of specific risk groups through a vector $\vec{p}$ with elements $0 < p_r < 1$ which takes

$$\sigma_r \to p_r \sigma_r, \qquad \tau_r \to p_r \tau_r \quad (\text{for Model One, } \sigma_r \to p_r \sigma_r)$$

This can then be used to examine the impact of targeting a risk group on the prevalence of HIV infection in the dynamical model.

The additional complexity of Model Two makes it possible to also consider interventions that target specific routes of infection, by reducing β_{Het}, β_{MF}, β_{MSM}, and/or β_{IDU}, which is heterosexual contact, sexual contact between females and MSM, sexual contact between MSM, and finally injecting drug use (sharing needles). As a real world application these interventions could be described as increasing the access to condoms in the case of sexual contact, and to clean needles in the case of injecting, or else simply reducing the number of acts that can potentially lead to the transmission of HIV. The interpretation of this is that if a rate β_x is modified to $p \times \beta_x$, then a proportion $(1-p)$ of acts associated with that transmission route, regardless of the risk groups involved, are made safe.

Parameterisation

This study considers the population of England and Wales and the models are parameterised based on this population. In the case of the first model this is stratified into four groups these being, heterosexual non-IDU, MSM non-IDU, heterosexual IDU and MSM–IDU. While for the second model, six groups are considered these being male and female heterosexuals (non-injecting), MSM (non-injecting), male and female IDUs, and MSM–IDU. We assume that a male heterosexual will only have sexual contact with females, while an MSM may have sexual contact both with other MSM and with females, which is in agreement with the findings from previous studies (Health Protection Agency, 2009; Johnson et al., 2001; Mercer et al., 2009). Mixing due to injecting can by definition only occur between those groups that are IDUs. In these models only those aged 15–49 have been considered. While it is acknowledged that there is likely to be some HIV transmission outside of this age group, almost all IDUs that were surveyed in the UA Surveys were aged 15–49, the overwhelming majority of at-risk behaviour will occur in this age group.

Behavioural data taken from the Unlinked Anonymous Monitoring surveys of IDUs undertaken by the Health Protection Agency (Noone et al., 1993; Health Protection Agency, 2009) is used to provide information on the IDU population of England and Wales particularly the size of the MSM–IDU population. Further secondary published data sources are used to provide information on the other populations and parameters for England and Wales. Table 1 shows the data sources used to parameterise this model while Table 2 shows the actual population estimates used. Model parameters are shown in Table 3, which also shows the values of the parameters when fitting the models to the data, prior to the implementation of the hypothetical intervention measures.

Since the surveys used were unlinked, and assortativity is known to be dynamically important (Garnett and Anderson, 1993), we vary the assortativity parameters in our sensitivity analysis. Nevertheless, we expect the more detailed parameters α_1 and α_2 of Model Two to sit between 0.5 and 1.0, and not at the extreme values, meaning that a 'baseline' of 0.75 is reasonable, provided model sensitivity to these parameters is also determined. However the value of α in Model One is harder to interpret and so our methodology is to fit this parameter to our choice for Model Two (using the mixing matrices shown in Fig. 2 as a criterion of similarity) and vary α in sensitivity analysis, which for each value taken during the sensitivity analysis the model is refit to the data.

Table 1
Parameter values for population and prevalence.

Parameter	Value	Reference
Population size estimates		
Total population in England and Wales aged 15–49	26,272,000	National Statistics Mid-2008 population estimates: www.statistics.gov.uk [accessed 05.09.11]
Proportion male	50.32%	=13,153,300 [National Statistics Mid-2008 population estimates]
Total IDU population	160,000	% England and Wales population currently injecting = 0.6% (Health Protection Agency, 2009; Sweeting et al., 2009)
% IDU male	76.5%	Current IDUs inject in the previous 4 weeks (Health Protection Agency, 2009)
% of males that are MSM	2.6%	Homosexual partners last 5 years aged 16–44 (Johnson et al., 2001)
% MSM in IDU population	2.24%	UA Surveys inject last 4 weeks 2007 data (Health Protection Agency, 2009)
Average IDU injecting career length	10 years	A number of references have given varying values for this parameter: 6 years (Sutton et al., 2005) and 11 years (Sweeting et al., 2009) for the UK and 8 years (Kaplan, 1989), 11 years (Pollack, 2001) and 20 years (Law et al., 2001a) for non-UK settings
HIV infection prevalence estimates		
Males (whole population)	0.17%	Health Protection Agency (2008a) for 15–59 years here (assumed the same for 15–49 years old here)
Females (whole population)	0.084%	Health Protection Agency (2008b) for 15–59 years here (assumed the same for 15–49 years old here)
MSM HIV prevalence	5.3%	Health Protection Agency (2008a) aged 15–44 (assumed the same for the larger age group applied here)
Male current IDUs in 2007	1.24%	UA Surveys 2007 (Health Protection Agency, 2009)
Female current IDUs in 2007	0.97%	UA Surveys 2007 (Health Protection Agency, 2009)
% MSM–IDU HIV positive	2%	UA Surveys 2007

Table 2
Estimated population sizes (rounded to nearest 100 for clarity).

Population	Total	Infected
Male heterosexual non-IDU	12,750,900	21,700
Female non-IDU	13,014,300	10,600
MSM	346,700	18,500
Male IDU	118,800	1400
Female IDU	37,600	400
MSM–IDU	3600	100

Figs. 1 and 2 (right hand side) show the mixing matrices for both Models One and Two at baseline. It can be seen that the mixing matrix for Model One is symmetrical which is due to the assumption that the susceptibility of infection for each group is equal to the transmissibility. Both models demonstrate increased risk of infection amongst IDU populations compared to both MSM and heterosexual populations, with the highest levels of mixing in Model Two being demonstrated for the IDU populations of the same type. Of interest is the level of mixing between female and male heterosexuals in Model Two. It can be seen that the transmission coefficient for females to males is higher than males to females; this possibly shows the impact of a small group of female sex workers amongst the much larger female heterosexual population.

In this study an arbitrary value of 50% has been used in all cases to measure the effectiveness of interventions that target specific populations, and specific transmission routes. It is acknowledged that in some cases this value can be regarded as large and therefore unrealistic, however it has been selected because in the case of some of the smaller populations, e.g. the IDU–MSM and IDU populations, surveillance studies have shown that high proportions of these individuals are in contact with treatment services (Health Protection Agency, 2010) and so it is likely that a 50% effectiveness could be achieved at a national level with comprehensive and intensive implementation of appropriate intervention measures. A 50% value is then implemented for easier comparison of the epidemiological significance of each risk group.

Results

The results here consider intervention measures that target different population groups against HIV, with particular focus on those that target the MSM–IDU population. A comparison of the results for Models One and Two will be considered, so that the impact of the model structure on the conclusions drawn from these models can be seen. Finally a sensitivity analysis examining the impact of key parameters on model results will also be undertaken.

Table 4 shows the impact of targeted intervention strategies that focus on making a proportion of individuals from a larger population sub-group safe from HIV infection. The results from both models are in agreement that targeting the IDU population leads to fewer cases of HIV being averted compared to targeting the MSM population. This is an unsurprising result given that in the England

Table 3
Dynamical model parameters.

Parameter	Symbol	Value	Notes
Model One			
Recruitment rate into population	Φ_{Hetro}	720,510	Fit to data
	Φ_{MSM}	9545.7	Fit to data
	$\Phi_{\text{Hetero IDU}}$	20,109	Fit to data
	$\Phi_{\text{MSM–IDU}}$	462.9	Fit to data
Assortativity	α	0.916	Fit to baseline for Model Two
Relative risk	ρ_{Hetero}	0.0840	
	ρ_{MSM}	2.2612	
	ρ_{IDU}	3.9099	
	$\rho_{\text{MSM–IDU}}$	11.162	
FOI scaling parameter	λ	1.51×10^{-8}	
Model Two			
Recruitment rate into population	$\Phi_{\text{M-hetro}}$	352,430	Fit to data
	$\Phi_{\text{F-hetro}}$	368,080	Fit to data
	Φ_{MSM}	9545.7	Fit to data
	$\Phi_{\text{M-IDU}}$	15274	Fit to data
	$\Phi_{\text{F-IDU}}$	4834.3	Fit to data
	$\Phi_{\text{MSM–IDU}}$	462.9	Fit to data
Sexual mixing between injecting groups	α_1	0.75	Selected baseline value (see text)
Injecting mixing between sex groups	α_2	0.75	Selected baseline value (see text)
Beta mixing matrix	β		See Fig. 2b
Sigma – susceptibility	$\sigma_{\text{M-hetero}}$	1	See text
	$\sigma_{\text{F-hetero}}$	0.188	Fit to data
	σ_{MSM}	0.175	Fit to data
	$\sigma_{\text{M-IDU}}$	1	See text
	$\sigma_{\text{F-IDU}}$	1.5	Fit to data
	$\sigma_{\text{MSM–IDU}}$	1	See text

Table 4
The number of HIV cases averted after 10 years following the interventions targeting the various model populations at 50% effectiveness (results shown for Models One and Two).

Population targeted	Heterosexual		MSM		IDU		MSM–IDU	
Model	One	Two	One	Two	One	Two	One	Two
Male-hetero		3202		115		512		12
Female-hetero		1514		503		161		6
Total heterosexual	4195	4716	1473	618	957	674	59	18
MSM	33	9	3461	3519	77	30	57	28
Male-IDU		8		26		861		23
Female-IDU		6		14		242		10
Total IDU	33	14	251	40	973	1103	11	33
MSM–IDU	3	0	23	53	7	41	36	37
Total cases averted	4264	4740	5209	4230	2014	1848	230	116
Cases averted/100 targeted	0.02	0.02	1.57	1.21	1.30	1.16	6.57	3.21

and Wales setting there is both a higher HIV prevalence in the MSM population compared with the IDU population and the MSM population is also larger. It can be seen that while targeting the MSM–IDU population results in the fewest number of HIV cases averted for both models, this is the most efficient intervention strategy in terms of cases averted per 100 individuals targeted with the intervention. This is in contrast to targeting the heterosexual population, which despite resulting in a large estimated number of HIV cases being averted; this is in fact a very inefficient approach when considering the very large number of individuals that need to be targeted with this intervention. It can be seen that there are differences between the model outputs of Model One and Model Two, this is likely to be due to the better structured sexual mixing that is described in Model Two. Fig. 3 shows the results obtained from Model Two over a ten year period, showing how the number of HIV cases averted in the various subgroups evolves over time.

The quantitative difference in the results between Models One and Two when targeting the MSM population shows the impact of the different assumptions about transmission routes in the population. What is most important here is that, despite the completely different model structure, the qualitative finding of relative efficiency in targeting the injecting MSM population is robust.

Fig. 4 shows the results obtained from Model Two considering the impact of targeting various HIV transmission routes with 50% of acts that carry a risk of HIV infection being made safe. Interestingly it can be seen that targeting heterosexual transmission in an England and Wales setting seems to lead to the greatest number of HIV cases averted over a 10 year period across all sub-groups (Fig. 4a), particularly amongst male heterosexuals. This is likely due to the higher prevalence of HIV amongst male heterosexuals compared to female heterosexuals. Again in agreement with the previous results (Table 4), targeting the MSM population is also quite an effective strategy, particularly if this were to include targeting transmission from MSM to females.

Sensitivity analysis

To investigate the impact of assortativity on model results, the impact of a variation in the assortativity parameter values on the

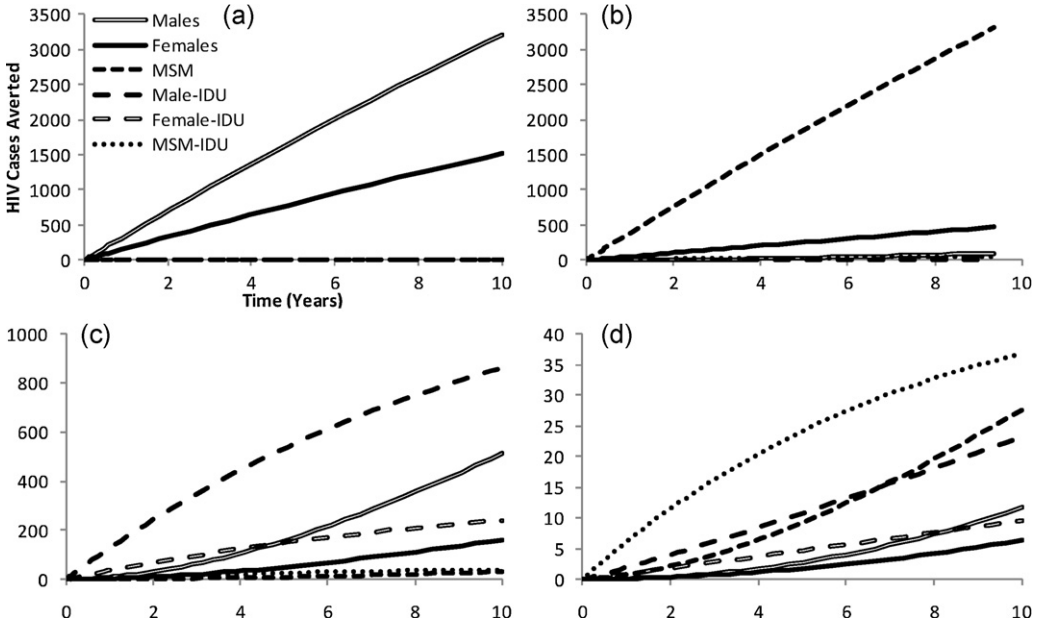

Fig. 3. Results obtained from Model Two showing the number of HIV cases averted following interventions targeting (a) heterosexuals; (b) MSM; (c) IDU; and (d) MSM–IDU at 50% effectiveness (note the differing scales on the *y*-axis).

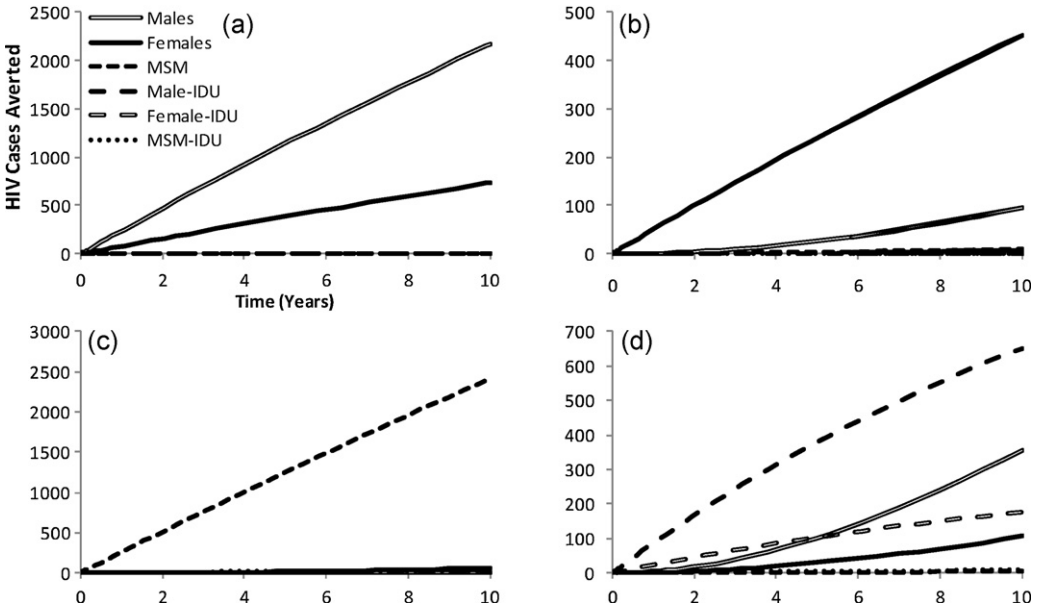

Fig. 4. Number of HIV cases averted with 50% of acts that carry a risk of HIV infection being made safe for transmission routes targeting: (a) heterosexual; (b) MSM to females; (c) MSM; and (d) IDU.

numbers of averted cases of HIV for the intervention targeting the MSM population is investigated, whereby the model is re-fit to the data for each new level of assortativity examined. This intervention has been selected for the sensitivity analysis as it provided differing results from Models One and Two using baseline parameters.

Model One assuming random mixing ($\alpha = 0$) results in 7814 HIV cases being averted over a 10 year period, while if it is assumed that there is virtually complete assortative mixing ($\alpha = 0.93$, above which the model would be inconsistent with the data as explained in detail in ESM) then 5171 HIV cases are found to be averted. In the case of Model Two, the impact of varying α_1 and α_2 on the number of averted cases of HIV is shown in Fig. 5 for both MSM and MSM–IDU interventions. It can be seen that in this case, while the assortativity parameters impact significantly on the model results, the variation of this impact on Model Two results is less than the impact of assortativity on Model One results. It also seems that in terms of relative numbers of cases averted, the MSM–IDU results are more sensitive to α_1 and α_2 than the MSM results, which is consistent with the hypothesis that the epidemiological significance of the MSM–IDU population lies in its role in mixing.

Discussion

In this research two simple models have been proposed that describe the transmission of HIV. The first model stratifies the general population into 4 groups, these being the heterosexual non-IDU population, heterosexual IDU population, MSM non-IDU population, and MSM–IDU population, while the second more complex model distinguishes between male and female heterosexuals and IDUs, leading to 6 different groups being described.

These models have been constructed with two aims. The first is to investigate the possible impact of interventions that target HIV transmission in the MSM and IDU populations, and the second aim is to investigate the impact of the model structure on the model results. These models have been implemented using data from a setting where the overall HIV prevalence is low but there is a higher prevalence amongst the MSM population, this being England and Wales. The results here from both models show the value of targeting the MSM–IDU population as this provides the highest number of HIV cases averted per 100 individuals targeted with an intervention. In the absence of other plausible explanations it is likely that it

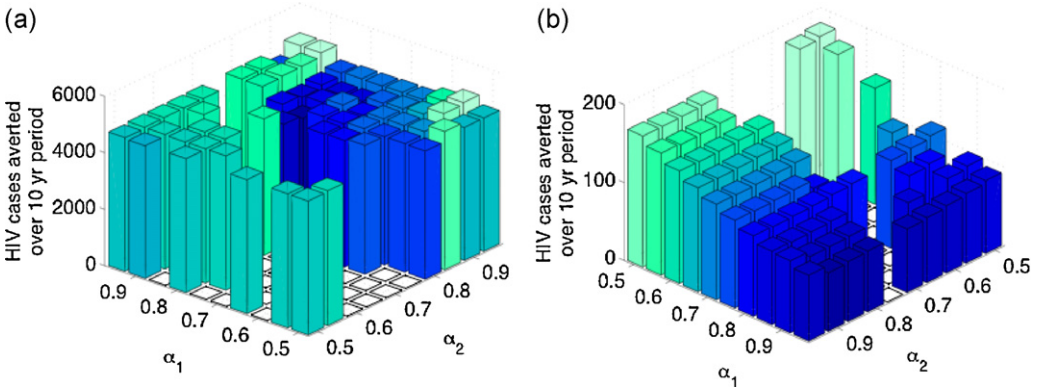

Fig. 5. The impact of varying the assortativity parameters in Model Two on the estimated HIV cases averted after 10 years for the intervention targeting the (a) MSM, (b) MSM–IDU population at 50% effectiveness. Only values consistent with the data (in the sense explained in ESM) are shown.

is efficient to target the MSM–IDU population because of the way in which this population bridges with other population sub-groups.

The level of assortativity can be very influential in determining the level and pattern of spread of infections such as HIV. High values of assortativity indicate that mixing mainly occurs within groups rather than between them, which leads to a less efficient spread of HIV. These have been shown to have an impact particularly on the estimated effectiveness of intervention measures that target small but very high-risk groups. However it is often very difficult to obtain data to inform precisely the level of mixing between groups, as this very often requires sophisticated and time consuming approaches to data collection such as chain-referral and other network sampling approaches (Kral et al., 2010).

It is acknowledged that the accuracy of the HIV prevalence estimates used here could be improved through a more comprehensive literature review utilising multiple data sources to obtain more accurate parameter values. The standard issue of identifiability for epidemic models is particularly important in this context – we have a vector (list) of prevalence estimates, but wish to know a matrix (table) of interactions and so there is insufficient data to parameterise the model without additional assumptions. For this study, our priority was to compare model predictions given different stratification and mixing structure, and therefore we overcame this identifiability problem essentially through model simplification. The results reported here were typically robust to model choice, but this may not be the case for research questions posed by future studies, meaning that model simplification is not a panacea for identifiability problems.

Furthermore, it is important to acknowledge that an arbitrary efficacy level of 50% reduction in transmission has been assumed whereas in reality this is often unknown and likely to vary between the measures and the targeted populations. Work aimed at informing public health policy directly should of course include realistic values for prevention efficacy. A final additional factor that has not been considered in this model is the possibility of individuals entering the model that have been infected elsewhere. In the context of England and Wales a significant proportion of heterosexually acquired HIV is due to infections that have occurred abroad prior to immigration to the UK (Health Protection Agency, 2008a). This suggests that the HIV FOI due to heterosexual transmission may be overestimated here, further suggesting that it may be even less efficient to target this group for interventions than the results from this model suggest. Future work could incorporate the immigration of infected individuals into the model population.

Two alternative intervention approaches have been considered in this study, targeting a proportion of individuals in the at-risk groups by removing a proportion from risk of infection, and targeting the transmission route itself. Over a ten year period it was found that removing individuals from risk of infection was generally the more effective approach to reducing HIV transmission. However it must be noted here, that in the case of sexual transmission, in reality this would be very difficult to achieve. It would seem hardly likely that people could be persuaded not to engage in any potentially risky sexual behaviour (which is what an intervention such as this would imply), although of course in the case of illicit drug use this is really the ultimate aim of most interventions and is more easily achieved, e.g. through opioid substitution treatment and needle and syringe programmes to increase the proportion of IDUs no longer at risk. It is likely that promoting testing is also important as this would lead to identifying those individuals that are infected and then providing target interventions to reduce risk behaviour with susceptibles in a manner that may lead to infection.

Previous models have incorporated a more accurate interpretation of the natural history of HIV infection (Grassly et al., 2003; Vickerman and Watts, 2002; Vickerman et al., 2006). However in this case to simplify the model structures it was decided to restrict the description of HIV infection to two groups these being either susceptible or infected, with no increased death rate imposed for the infected class. It is acknowledged that without accurately representing the natural history of infection it becomes impossible to investigate the timing of interventions that target individuals that are recently infected, and therefore highly infectious following their recent infection. The absence of the death rate in England and Wales can be justified given the increased risk of short term mortality due to HIV in older adults in this setting (Smith et al., 2010). In England and Wales, there is good access to testing and treatment and consequently those diagnosed with HIV can access treatment and care.

There are of course many opportunities to make the simple models proposed here more realistic. While these models have their uses in terms of providing a basic understanding of the impact of assortativity and of the potential impact of selected interventions, these of course cannot be applied in their correct state to investigate alternative interventions that target more specific behaviour such as a reduction in the number of injecting events or unprotected sex acts (although these interventions were implied when considering the interventions targeting the transmission routes). Additionally these models have not considered the diagnosed status of those individuals infected by HIV. This may have important implications for treatment and transmission, given that an uninfected individual is less likely to have unsafe sex with a person diagnosed with HIV than with someone undiagnosed (Law et al., 2001b).

This study has only considered England and Wales which is a low HIV prevalence setting and as such the results from this model are very much particular to this location. However given their simplicity, these models could easily be applied to other settings providing that the data required is available.

Conclusion

This study here has shown the value of targeting the MSM population with interventions to reduce their at-risk behaviour, with the results suggesting that this will have a positive impact on the reduction in the number of cases of HIV in England and Wales. In particular targeting the MSM–IDU population was found to be a relatively efficient measure given that this had the highest number of cases averted per 100 individuals targeted, suggesting that this may also be the most cost-effective approach as well. Additionally it was found that while targeting interventions at the level of the general population resulted in the most cases averted, this was the least efficient approach. However for the purpose of making like-for-like comparisons it has been assumed in this study that all the interventions were equally effective. This assumption can be updated in future studies. The results here have also shown the importance of the assumed assortativity of mixing between population groups on the model results.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.epidem.2011.12.001.

References

Diekmann, O., Heesterbeek, J.A.P., 2000. Mathematical epidemiology of infectious diseases – model building analysis and interpretation. John Wiley & Sons Ltd., New York.

Garnett, G.P., Anderson, R.M., 1993. Factors controlling the spread of HIV in heterosexual communities in developing countries: patterns of mixing between different age and sexual activity classes. Philos. Trans. R. Soc. Lond. B: Biol. Sci. 342, 137–159.

Grassly, N.C., Lowndes, C.M., Rhodes, T., Renton, A., Garnett, G.P., 2003. Modelling emerging HIV epidemics: the role of injecting drug user and sexual transmission in the Russian Federation, China and India. Int. J. Drug Policy 14, 25–43.

Health Protection Agency. HIV in the United Kingdom. London; 2008.

Health Protection Agency. Sexually transmitted infections and men who have sex with men in the UK. London; 2008.

Health Protection Agency, Health Protection Scotland, Public Health Wales, CDSC Northern Ireland, CRDHB. Shooting up: infections among injecting drug users in the United Kingdom. London; 2009.

Health Protection Agency, Health Protection Scotland, Public Health Wales, CDSC Northern Ireland, CRDHB. Shooting up: infections among injecting drug users in the United Kingdom. London; 2010.

Hope, V.D., Rogers, P.A., Jordan, L., Paine, T.C., Barnett, S., Parry, J.V., Gill, O.N., 2002. Sustained increase in the sharing of needles and syringes among drug users in England and Wales. AIDS 16, 2494–2496.

Johnson, A.M., Mercer, C.H., Erens, B., Copas, A.J., McManus, S., Wellings, K., Fenton, K.A., Korovessis, C., Macdowall, W., Nanchahal, K., Purdon, S., Field, J., 2001. Sexual behaviour in Britain: partnerships, practices, and HIV risk behaviours. Lancet 358, 1835–1842.

Kaplan, E.H., 1989. Needles that kill: modeling human immunodeficiency virus transmission via shared drug injection equipment in shooting galleries. Rev. Infect. Dis. 11, 289–298.

Kral, A.H., Malekinejad, M., Vaudrey, J., Martinez, A.N., Lorvick, J., McFarland, W., Raymond, H.F., 2010. Comparing respondent-driven sampling and targeted sampling methods of recruiting injection drug users in san francisco. J. Urban Health 87, 839–850.

Law, M.G., Lynskey, M., Ross, J., Hall, W., 2001a. Back-projection estimates of the number of dependent heroin users in Australia. Addiction 96, 433–443.

Law, M.G., Prestage, G., Grulich, A., Van de Ven, P., Kippax, S., 2001b. Modelling the effect of combination antiretroviral treatments on HIV incidence. AIDS 15, 1287–1294.

Mercer, C.H., Hart, G.J., Johnson, A.M., Cassell, J.A., 2009. Behaviourally bisexual men as a bridge population for HIV and sexually transmitted infections? Evidence from a national probability survey. Int. J. STD AIDS 20, 87–94.

Noone, A., Durante, A.J., Brady, A.R., Majid, F., Swan, A.V., Parry, J.V., Hart, G.J., Connell, J.A., Perry, K.R., Joce, R.E., 1993. HIV infection in injecting drug users attending centres in England and Wales, 1990–1991. AIDS 7, 1501–1507.

Pollack, H.A., 2001. Cost-effectiveness of harm reduction in preventing hepatitis C among injection drug users. Med. Decis. Making 21, 357–367.

Smith, R.D., Delpech, V.C., Brown, A.E., Rice, B.D., 2010. HIV transmission and high rates of late diagnoses among adults aged 50 years and over. AIDS 24, 2109–2115.

Strathdee, S.A., Stockman, J.K., 2010. Epidemiology of HIV among injecting and non-injecting drug users: current trends and implications for interventions. Curr. HIV/AIDS Rep. 7, 99–106.

Sutton, A.J., Gay, N.J., Edmunds, W.J., Andrews, N.J., Hope, V.D., Gill, O.N., 2005. Modelling the characteristics of the male injecting drug user population in England and Wales. Int. J. Drug Policy 16, 176–182.

Sutton, A.J., Gay, N.J., Edmunds, W.J., 2006. Modelling the impact of prison vaccination on hepatitis B transmission within the injecting drug user population of England and Wales. Vaccine 24, 2377–2386.

Sweeting, M., De Angelis, D., Ades, A., Hickman, M., 2009. Estimating the prevalence of ex-injecting drug use in the population. Stat. Methods Med. Res. 18, 381–395.

van de Laar, M.J., Likatavicius, G., 2009. HIV and AIDS in the European Union, 2008. Euro Surveill., 14.

Vickerman, P., Watts, C., 2002. The impact of an HIV prevention intervention for injecting drug users in Svetlogorsk, Belarus: model predictions. Int. J. Drug Policy 13, 149–164.

Vickerman, P., Hickman, M., Rhodes, T., Watts, C., 2006. Model projections on the required coverage of syringe distribution to prevent HIV epidemics among injecting drug users. J. Acquir. Immune Defic. Syndr. 42, 355–361.