THE LANCET

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Web Appendix –technical appendix, summary stats, references for the technical appendix & additional refs

Technical specification of the mathematical simulation model

The methods will be described in the following three parts: (i) the technical specification of the mathematical simulation model used for Odessa and Karachi; (ii) the analytic framework; (iii) the data and sources for parameter values; and, (iv) Methods for Nairobi IDU modelling.

Technical Specification of Mathematical Simulation Model

Differential equations

The model is specified by a set of ordinary differential equations which are solved numerically using custom-made software developed by the authors. They are formed as follows and illustrated in Figure 1:

$$\frac{dX^1_{k,i,j}(t)}{dt} = R\phi_{k,i,j} - \lambda_{k,i,j}X^1_{k,i,j} - \mu X^1_{k,i,j}$$

$$\frac{dX^2_{k,i,j}(t)}{dt} = \lambda_{k,i,j}X^1_{k,i,j} - (\sigma_2 + \mu)X^2_{k,i,j}$$

$$\frac{dX^3_{k,i,j}(t)}{dt} = \sigma_2 X^2_{k,i,j} - (\sigma_3 + \mu)X^3_{k,i,j}$$

$$\frac{dX^4_{k,i,j}(t)}{dt} = (1 - a_{350}(t))\sigma_3 X^3_{k,i,j} - (\sigma_4 + \mu)X^4_{k,i,j}$$

$$\frac{dX^5_{k,i,j}(t)}{dt} = (1 - a_{200}(t))\sigma_4 X^4_{k,i,j} - (\sigma_5 + \mu)X^5_{k,i,j}$$

$$\frac{dX^6_{k,i,j}(t)}{dt} = \sigma_5 X^5_{k,i,j} + -(\sigma_6 + \mu)X^6_{k,i,j}$$

$$\frac{dX^7_{k,i,j}(t)}{dt} = \sigma_6 X^6_{k,i,j} + \sigma_8 X^8_{k,i,j} - (\sigma_7 + \mu)X^7_{k,i,j}$$

$$\frac{dX^8_{k,i,j}(t)}{dt} = a_{350}(t)\sigma_3 X^3_{k,i,j} + a_{200}(t)\sigma_4 X^4_{k,i,j} - (\sigma_8 + \mu)X^8_{k,i,j}$$

The state variables are given by $X^s_{k,i,j}(t)$: *t* is the time elapsed in the simulation; *s* is the infection-status (1= susceptible; 2= acute infection; 3= latent infection with CD4>350; 4= latent infection with CD4 between 200 and 350; 5= pre-AIDS with CD4<200; 6=pre-AIDS with elevated viral load; 7= AIDS; 8=on ART), *k* is 'type' (1= men who sex with women; 2= women; 3=male bisexuals; 4=Men who have sex with men (MSM)), *i* is injecting equipment usage behaviour (1=does not use non-sterile equipment; 2= "rarely" uses non-sterile equipment; 3= "often" uses non-sterile equipment), and *j* is sexual behaviour (1=does not have unprotected sex; 2=has “few” sex partners; 3=has “many” sex partners, including sex workers). In the description that follows, a dot (•) in the position of any of these indices indicates a sum across that index.

$\phi_{k,i,j}$ is the fraction of those starting injecting drugs of that type and behaviour; $1/\sigma_s$ is the mean time spent in infection phase *s*; $\lambda_{k,i,j}$ is the force of infection for individuals of that type and behaviour; μ is the rate of exiting the IDU population, and incorporates non-HIV related mortality (M) and mean time spent injecting drugs (L): $\mu = M + 1/L$. R is the rate of entry of the IDU population, and is set so as to maintain a constant population size, such that: $R = \mu X^{\bullet}_{\bullet,\bullet,\bullet} + \sigma_6 X^{7}_{\bullet,\bullet,\bullet}$. $a_{350}(t)$ and $a_{200}(t)$ are the proportion of individuals with CD4 cell count 350 and 200, respectively, that are initiated on treatment at that time.

The boundary conditions of the system are:

$$X^{1}_{k,i,j}(0) = (1 - seed)\phi_{k,i,j} N_0$$
$$X^{3}_{k,i,j}(0) = (seed)\phi_{k,i,j} N_0$$

N_0 is the size of IDU population at the start of the simulation and $seed$ is the HIV prevalence at the start of the simulation in all parts of the population.

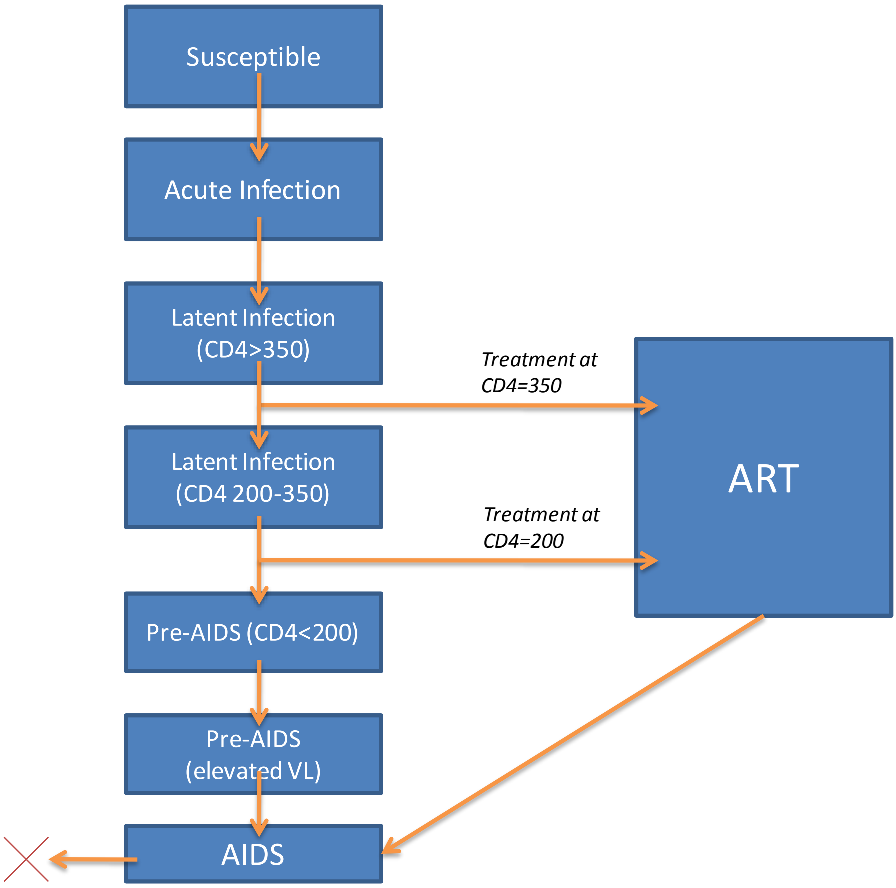

Figure S1: Flow diagram showing how the course of HIV infection is represented in the simulation model.

The structure of $\phi_{k,i,j}$ is as follows:

$$\phi_{k,i,j} = K_k I_i J_{k,j}$$

Where K_k is the proportion of IDU of that type; I_i is the proportion of IDU with that injecting equipment usage behaviour; and, $J_{k,j}$ is the proportion of IDU of that type in that sexual risk group.

Calculation of Force of Infection

$\lambda_{k,i,j}$ is the force of infection for individuals of that type, injecting equipment usage behaviour and sexual behaviour. It combines the risk of HIV infection through use of contaminated injecting equipment (λ_i^{idu}) and through sex ($\lambda_{k,j}^{sex}$): $\lambda_{k,i,j} = \lambda_i^{idu} + \lambda_{k,j}^{sex}$.

The force of infection through using injecting equipment depends on, the pattern of usage of non-sterile equipment with respect to frequency of either leaving equipment where others may use it or intentionally sharing with others ($\rho_{i,i'}^{idu}$), the infected-status and infectiousness of individuals with whom the equipment is shared (p_i^{idu}), the fraction of shared equipment that is cleaned (δ^{idu}) and the efficacy of cleaning in removing the risk of HIV transmission (α^{idu}).

$$\lambda_i^{idu} = \sum_{i'} \rho_{i,i'}^{idu} p_{i'}^{idu}.$$

$$p_i^{idu} = \frac{\beta_0^{idu}\left(1-\delta^{idu}\alpha^{idu}\right)\sum_{s=2}^{6}\beta_s X_{\bullet,i,\bullet}^{s}}{\sum X_{\bullet,i,\bullet}^{\bullet}}$$

β_0^{idu} is the chance of HIV transmission per use of contaminated injecting equipment if the equipment was last used by an individual with latent HIV infection. β_s is the *relative* infectiousness of individuals in HIV stage *s*, compared to those with latent infection.

$\rho_{i,i'}^{idu}$ is the number of times equipment is shared with individual in usage group *i* with individuals in group *i'*. Following others (1), the extent to which sharing is random or assortative with respect to sharing behaviour is determined with a single mixing parameter (ε^{idu}):

$$\rho_{i,i'}^{idu} = \left(\left(1-\varepsilon^{idu}\right)\left(\frac{c_{i'}X_{\bullet,i',\bullet}^{\bullet}}{\sum_{i'} c_{i'}X_{\bullet,i',\bullet}^{\bullet}}\right)+\varepsilon^{idu}Q_{i,i'}\right)c_i$$

c_i is the number of times injecting equipment is shared by those in that sharing behaviour group.

$Q_{x,y}$ =1 if $x = y$, and 0 otherwise. ε^{idu} would be closer to 1.0 if, for instance, in most cases of individuals using non-sterile equipment that equipment is found discarded by someone else; ε^{idu} would be closer to 0.0 if, in most cases, individuals using non-sterile equipment are using the equipment lent to them by someone they know and with whom they often inject.

The force of infection through sexual contact depends on, the pattern of sexual partnership formation with respect to type and sexual-risk behaviour ($\rho^{sex}_{k,j,k',j'}$), the infection-status and stage of infection of the partner ($p^{sex}_{k,k',j,j'}$), the fraction of sex acts in which a condom is used ($\delta_{k,k',j,j'}{}^{sex}$) and the efficacy of condoms in reducing the risk of HIV transmission (α^{sex}).

$$\lambda^{sex}_{k,j} = \sum_{k',j'} \rho^{sex}_{k,j,k',j'} p^{sex}_{k,k',j,j'}$$

$$p^{sex}_{k,k',j,j'} = 1 - \left(1 - \frac{\sum_{s=2}^{6} \beta_0^{sex} \gamma_{k,k'} \left(1 - \delta^{sex}_{k,k',j,j'} \alpha^{sex}\right) \beta_s X^{s}_{k',\bullet,j'}}{X^{\bullet}_{k',\bullet,j'}} \right)^{w_{j,j'}}$$

$p^{sex}_{k,k',j,j'}$ itself depends on infected-status and infectiousness of partners and rate of sex acts in such a partnerships (number per partner per year: $w_{j,j'}$). The rate of sex acts in a partnership is set at three levels: (i) rate of sex acts in partnerships between those that have “few” partnerships ($w_{2,2}$), (ii) rate of sex acts in partnerships between those have “few” partnerships and those that have “many” partnerships ($w_{2,3} = w_{3,2}$), and (ii) rate of sex acts in partnerships between those have “many” partnerships ($w_{3,3}$). The frequency of condom use is partnerships is set at four levels according to the type partnership: (i) sex between a man and a woman who each have “few” partnerships ($\delta^{sex}_{1,2,2,2} = \delta^{sex}_{2,1,2,2} = \delta^{sex}_{3,2,2,2} = \delta^{sex}_{2,3,2,2}$); (ii) sex between a man and a woman and either or both have “many” partnerships ($\delta^{sex}_{1,2,3,j'} = \delta^{sex}_{1,2,2,3} = \delta^{sex}_{2,1,3,j'} = \delta^{sex}_{2,1,2,3}$); (iii) sex between two men and both have “few” partnerships ($\delta^{sex}_{3,3,2,2} = \delta^{sex}_{3,4,2,2} = \delta^{sex}_{4,3,2,2} = \delta^{sex}_{4,4,2,2}$); and (iv) sex between two men and either or both have “many” partnerships

($\delta^{sex}_{3,3,3,j'} = \delta^{sex}_{3,4,3,j'} = \delta^{sex}_{4,3,3,j'} = \delta^{sex}_{4,4,3,j'} = \delta^{sex}_{3,3,2,3'} = \delta^{sex}_{3,4,2,3} = \delta^{sex}_{4,3,2,3} = \delta^{sex}_{4,4,2,3}$).

β_0^{sex} is the chance of HIV transmission per sex act if the sex act was with an individual with latent HIV infection. $\gamma_{k,k'}$ is the relative chance of transmission in partnership between individuals of these two types, relative to female-to-male chance of transmission: (female-to-male $\gamma_{1,2}$; male-to-female $\gamma_{2,1}$; MSM-to-Bisexual or Bisexual to MSM $\gamma_{3,4} = \gamma_{4,3}$; Bisexual male-to-female $\gamma_{2,3}$).

Mixing matrices are constructed for sex between men (including bisexual men) and women and for sex between MSM and bisexual men. The total number of sex partners per year is $d_{k,j}$, of which a proportion υ_j are formed with other injecting drug users and a proportion of bisexual's partnerships (η) are with women.

The distribution of men's partnerships across women in different groups:

$$\chi_{1,j,j'} = \left((1-\varepsilon^{sex}) \frac{\upsilon_{j'} d_{1,j'} X^{\bullet}_{2,\bullet,j'}}{\sum_{j'} \upsilon_{j'} d_{2,j'} X^{\bullet}_{2,\bullet,\bullet}} + \varepsilon^{sex} Q_{j,j'} \right)$$

The distribution of women's partnerships across men (including bisexual men) in different groups:

$$\chi_{2,j,j'} = \left((1-\varepsilon^{sex}) \frac{\upsilon_{j'} \left(d_{1,j'} X^{\bullet}_{1,\bullet,j'} + \eta d_{3,j'} X^{\bullet}_{3,\bullet,j'} \right)}{\sum_{j'} \upsilon_{j'} \left(d_{1,j'} X^{\bullet}_{1,\bullet,\bullet} + \eta d_{3,j'} X^{\bullet}_{3,\bullet,\bullet} \right)} + \varepsilon^{sex} Q_{j,j'} \right)$$

These two expressions need to 'balance' so that the number of each type partnership between men and women in different groups formed is consistent in the force of infection to men and to women. In the event of a discrepancy, the extent to which a balanced matrix reflects the original version for the men, is determined by θ.

$$D_{q,jm,jf} = \frac{\left(d_{1,j} X^{\bullet}_{1,\bullet,\bullet} + d_{3,j} X^{\bullet}_{3,\bullet,\bullet} \right) \upsilon_{jm} \chi_{1,jm,jf}}{X^{\bullet}_{2,\bullet,\bullet} \chi_{2,jf,jm} \upsilon_{jf} d_{2,jf}}$$

$$\chi_{1,j,j'} \rightarrow \chi_{1,j,j'} D_{q,jm,jf}^{-(1-\theta)}$$

$$\chi_{2,j,j'} \rightarrow \chi_{2,j,j'} D_{q,jf,jm}^{\theta}$$

$$\chi_{3,j,j'} = \chi_{4,j,j'} = \left(1-\varepsilon^{sex}\right)\left(\frac{(1-\eta)\upsilon_{j'}d_{3,j'}X^{\bullet}_{3,\bullet,j'} + d_{4,j'}\upsilon_{j'}X^{\bullet}_{4,\bullet,j'}}{\sum_{j'}(1-\eta)\upsilon_{j'}d_{3,j'}X^{\bullet}_{3,\bullet,j'} + d_{4,j'}\upsilon_{j'}X^{\bullet}_{4,\bullet,j'}}\right) + \varepsilon^{sex}Q_{j,j'}$$

The fraction of womens' partnerships that are formed with bisexuals is: $m_j = \frac{\eta d_{3,j'}X^{\bullet}_{3,\bullet,j'}}{d_{1,j'}X^{\bullet}_{1,\bullet,j'} + \eta d_{3,j'}X^{\bullet}_{3,\bullet,j'}}$.

The fraction of MSMs' partnership that are formed with with bisexuals is: $n_j = \frac{(1-\eta)\upsilon_{j'}d_{3,j'}X^{\bullet}_{3,\bullet,j'}}{(1-\eta)\upsilon_{j'}d_{3,j'}X^{\bullet}_{3,\bullet,j'} + d_{4,j'}\upsilon_{j'}X^{\bullet}_{4,\bullet,j'}}$.

The full mixing matrix is then defined as follows, with elements equal to zero otherwise.

$$\rho^{sex}_{1,j,2,j'} = \upsilon_j d_{1,j}\chi_{1,j,j'}$$
$$\rho^{sex}_{2,j,1,j'} = (1-m_j)\upsilon_j d_{2,j}\chi_{2,j,j'}$$
$$\rho^{sex}_{2,j,3,j'} = m_j\upsilon_j d_{2,j}\chi_{2,j,j'}$$
$$\rho^{sex}_{3,j,2,j'} = \eta_j\upsilon_j d_{3,j}\chi_{1,j,j'}$$
$$\rho^{sex}_{3,j,4,j'} = (1-\eta_j)\upsilon_j d_{3,j}\chi_{3,j,j'}$$
$$\rho^{sex}_{4,j,3,j'} = n_j\upsilon_j d_{4,j}\chi_{4,j,j'}$$
$$\rho^{sex}_{4,j,4,j'} = (1-n_j)\upsilon_j d_{4,j}\chi_{4,j,j'}$$

Analytic Framework

For this simulation model there are two sources of prior information: information on the model parameters, including details about HIV natural history and HIV-risk behaviour, and information on HIV prevalence. The Bayesian Melding procedure (2) combines these sources of information on the inputs and outputs, respectively. The information on prevalence is distinguished from the actual data on prevalence because it can be based on expert opinion or indirectly on data that is not perfectly comparable.

Following the procedure and notation proposed by Alkema *et al.* (3), we denote the simulation model described above as M , the model input parameters as $\boldsymbol{\theta}$ (including all the parameters listed in Table 1) and the model output (HIV prevalence over time in the general population) as $\boldsymbol{\rho}$. That is, $\boldsymbol{\rho} = M(\boldsymbol{\theta})$. We denote the direct priors (information on HIV prevalence rates) as $p(\boldsymbol{\rho})$. We allow this information to be in the form of intervals for HIV prevalence at certain times. In this way, the direct prior can only either support or refute a particular simulated epidemic curve. This is represented formally by:

$$p(\boldsymbol{\rho}) \propto \prod_{t \in \Gamma} I_{V_t}(\rho_t)$$

Where Γ is the set of years for which there is prior knowledge, V_t is the specified interval for prevalence in year t, and $I_A(x)$ is the indicator function (equals 1 if $x \in A$ (x is included in A), or 0 otherwise).

For each input model parameter, available information is summarised in the prior marginal distribution (for details see below). The prior density for each set of parameters is denoted $p(\theta)$. This translates to an induced prior on model outputs, which is denoted $p^*(\boldsymbol{\rho})$.

The two sources of prior information are combined to give a pooled prior $\tilde{p}(\boldsymbol{\rho})$:

$$\tilde{p}(\boldsymbol{\rho}) \propto p^*(\rho) \prod_{t \in \Gamma} I_{V_t}(\rho_t)$$

Next, we denote the data on HIV prevalence as $\mathbf{W}$. The fundamental Bayesian relationship between the prior information, the data and the updated posterior information can be expressed as:

$$p(\boldsymbol{\rho} | \mathbf{W}) \propto \tilde{p}(\boldsymbol{\rho}) p(\mathbf{W} | \boldsymbol{\rho})$$

Since the model is not invertible, it is not possible to derive an analytic solution with which to calculate the posterior distributions. A standard 'Monte Carlo' technique is used to approximate this instead; a modified Sample-Importance-Resample algorithm (4). This consists of the following steps:

1. Generate a set of parameters by sampling from the prior distributions of each parameter: $\boldsymbol{\theta}^{(i)}$. To increase efficiency, a stratified without-replacement sampling scheme is used, with appropriate correction for the weighting made throughout (5). Form the prior for this set of parameter values: $p(\theta)$.
2. Evaluate the model using this set of parameters: $\boldsymbol{\rho}^{(i)} = M\left(\boldsymbol{\theta}^{(i)}\right)$
3. Form the sampling weight for the run as the product of the likelihood and the pooled prior: $\omega_i = p\left(\mathbf{W} | \boldsymbol{\rho}^{(i)}\right) \tilde{p}(\boldsymbol{\rho}^{(i)})$
4. Repeats steps 1-3, N times.

5. Re-sample from the discrete distributions of epidemic simulations Q times, with probability proportional to the sampling weights, to approximate the posterior distribution for the inputs.

The likelihood of the simulated epidemic given the prevalence data, $p(\mathbf{W}|\boldsymbol{\rho})$, is estimated assuming only binomial errors in the estimate and independence between samples (6):

$$p(\mathbf{W}|\boldsymbol{\rho}) \propto \prod_i \rho(t_i)^{y_i N_i} (1-\rho(t))^{(1-y_i)N_i}$$

Where $\rho(t)$ is the model HIV prevalence at time t and the i th observation is at time t_i, records a prevalence of y_i and is from a sample of size N_i.

In this process, the number of samples, N, must be large so that combinations of parameters are selected from all regions of the multi-dimensional parameter space. In experimental analyses, a value for N was found by examining how changes in model fits and conclusions changed with increasing values of N.

The posterior distribution for the inputs ($p(\boldsymbol{\rho}|\mathbf{W})$) provides the baseline "fit" of the model to the observed epidemic. This is used to generate estimate of the course of HIV epidemic in the IDU population and associated bounds of uncertainty. The impact of interventions on the HIV epidemic is represented by modifying certain of the parameter values at a defined point in the simulation. To quantify the impact these changes would have on HIV incidence, the same 'intervention manipulation' is applied to each of the items in the posterior set, and the change in incidence is calculated relative to the corresponding baseline run. This generates a distribution of effect size, which reflects the uncertainty in the model specification/parameterisation, but not the uncertainty in the expected size of the intervention. The impact of alternative types of interventions and combinations of interventions are then explored scenario-wise systematically, as described in the main text.

Parameter Values

The parameters in the model are in the following categories:

1. <u>Parameters that define the natural history of HIV (survival, infectiousness).</u>

These parameters are evaluated from the general scientific literature and generalised across all settings: values are provided in Table 1. For reasons of computational efficiency, but with the exception of β_0^{idu} and β_0^{sex}, the uncertainty in these parameter values is not reflected in the estimates of uncertainty of the intervention impact.

2. <u>Parameters that describe the basic demography of IDU populations (population size, mortality rate).</u>

These parameters are specific to each setting but are not using in the model 'fitting' procedure (defined below) because they are non-informative. However, in the estimates of projections of incidence rates, uncertainty in the estimated size of the population is captured (7).

3. <u>Parameters that describe the distribution of risk in the population.</u>

These parameters are specific to each setting. Their value is estimated in Bayesian framework using prior information from a literature review and HIV prevalence estimates (see Tables that follow). For each parameter, a prior distribution is defined reflecting uncertainty in the information about that parameter – including, but not limited to, uncertainty arising through random sampling errors.

4. <u>Parameters that describe the impact of structural changes and interventions.</u>

These parameters are specific to each setting and characterise how certain structural changes could potentially affect proximate determinants of risk and influence the course of the epidemic. These are evaluated as follows:

Odessa: The potential impact of changing the policing practices was quantified by examining the relationship between key indicator of risk behaviour in the last 30 days ('using preloaded syringes', 'front/back-loading a syringe' and 'receptive needle sharing') and reporting ever being beaten by police, among a study of 600 IDU in Odessa in 2004-7 (8). The impact of police beatings on the epidemic was thus estimated by measuring the extent to which the overall frequency of each type of risk could be attributed to ever being beaten. In Odessa, 24% of IDU reported ever being by police and, for instance, 22% of those that had also reported using preloaded syringes in the last years compared to 6% of those who had never been beaten. It was thus estimated that without police beatings, there would be a 29% reduction in use of non-sterile equipment, on the basis that, compared to the population overall, individuals who had never been beaten were, on average, 29% less likely to have report each form of risky exposure. The analysis was repeated using data from the same study conducted in the cities of Makeevka and Kiev. In these settings, the frequency of reporting ever being beaten for police was higher (Makeevka: 46%; Kiev 55%) but the individual-level association being beaten and risk behaviour was weaker. The overall estimated reduction in risk associated with removal of police beatings in these settings was 16% for Makeevka and 10% for Kiev.

Karachi: The impact on the epidemic of non-injecting drug users transitioning to injecting drugs was explored. Assuming that between 15% and 30% of all drug users are currently injecting users (9), and that there are approximately 9000 IDU in Karachi (see Tables below), it was estimated that there would be between 30,000 and 60,000 total drug users in Karachi. The model simulated that, in one year, 8%, 10% or 12% of non-injecting drug users, become injecting-users. This corresponds to 3600, 4500 or 5400 individuals transitioning to the IDU population.

Assumed Efficacy of OST/NEP Interventions in Both Settings:

Needle Exchange Programmes: Based on a review by Wodak and Cooney (2006) (10), we assume that individuals in contact with NEP, on average, reduce the rate of using non-sterile equipment by 50%. No effect on sexual risk behaviour is assumed to result from contact with NEP.

Opioid Substitution Treatment: We assume that availability of OST reduces injection frequency and needle sharing by 50%, based on a range of observational studies indicating reductions in the rate of receptive needle sharing between 33 and 67% (11-14). This range is considered to capture the effects of drop-out from programmes, which can impair the efficacy compared with perfection retention of those on treatment (15, 16). Effectiveness of methadone and buprenorphine is assumed equivalent, since studies show no significant differences. Although, some studies show reductions in the number of sex partners and/or increases in condom use associated with methadone maintenance, it is not clear that any effect is substantial or maintained, and here no effect on sexual behaviour of OST is assumed.

Parameter	Symbol	Value	Source/Comments
Relative rate of HIV transmission per sex act: female-to-male (vs. female-to-male).	$\gamma_{1,2}$	1	Definition.
Relative rate of HIV transmission per sex act: male-to-female vs. (vs. female-to-male).	$\gamma_{2,1}$	2	(17)
Relative rate of HIV transmission per sex act: male-to-male (vs. female-to-male).	$\gamma_{3,4} = \gamma_{4,3}$	10	(18)
Mean duration of acute phase infection.	$1/\sigma_2$	3 months	(19)
Mean interval between end of acute infection and CD4=350	$1/\sigma_3$	4.55	(20)
Mean interval between CD4=350 and CD4=200	$1/\sigma_4$	4.6	(19, 20)
Mean interval between CD4=200 and elevation in viral load	$1/\sigma_5$	1.1	(Fitted to provide consistency between (20), (21) and (19)
Mean interval with elevated viral load with pre-AIDS	$1/\sigma_6$	10 months	(19)
Mean interval with AIDS before death	$1/\sigma_7$	9 months	(19)
Mean duration of viral suppression of ART.	$1/\sigma_8$	7.5 years	(22)
Average transmission rate of HIV per use of non-sterile equipment (if last person to use had latent HIV infection).	β_0^{idu}	~0.0085	Uncertainty is reflected in estimates of intervention impact. (17)
Average transmission rate of HIV per sex act (if partners had latent HIV infection).	β_0^{sex}	~0.0038	Uncertainty is reflected in estimates of intervention impact. (23)
Relative infectiousness of individuals in acute phase infection (vs. latent infection).	β_2	27	(19)
Relative infectiousness of individuals in latent phase infection (vs. latent infection).	β_3	1	Definition.
Relative infectiousness of individuals in pre-AIDS phase infection (vs. latent infection).	β_4	7	(19)
Relative infectiousness of individuals in AIDS phase infection (vs. latent infection).	β_5	0	(19)
Relative infectiousness of virally-suppressed individuals on ART (vs. latent infection).	β_6	0.08	(24)

Table S1: HIV natural history parameters that do not vary between settings.

ODESSA, UKRAINE					Distribution of prior				
Parameter Number	**Parameter Name**	**Symbol**	**Description**	**Estimate**	**Shape**	**"a"**	**"b"**	**"c"**	**Comments**
1	IDUPop	N_0	Number of IDU.	16268	Triangle	15120	17100	16268	Median and lower and upper bounds of estimates of IDU population size in Odessa (25).
2	MortRate	M	Mortality rate of IDU.	0.04	Fixed	-99	-99	-99	Survey of IDU in Odessa 2001, as reported in Vickerman et al (26).
3	DurIDU	L	Mean duration (years) spent as IDU.	35.00	Uniform	20	50	-99	Based on observation of 5% of IDU in Odessa started in last year (Vickerman et al. STD 2006) and 2% started in last year in study of Odessa IDUs (n=600) conducted from 2004-07 (8).
4	Pr_IDU_IsMen	$K_1 + K_2 + K_3$	Fraction of IDU that are men.	0.70	Triangle	0.65	0.8	0.7	Survey of IDU in Odessa 2001, as reported in Vickerman et al (26).and range from review of other studies in Ukraine.
5	Pr_IDURisk_None	I_1	Fraction of IDU that never share needles.	0.53	Uniform	0.488	0.568	0.528	Estimate and 95% confidence interval limits from study of Odessa IDUs (n=600) conducted from 2004-07 (8).

6	Pr_IDURisk_High	$I_3/(I_2+I_3)$	Fraction of IDU that ever share needles, that do so often.	0.24	Uniform	0.19	0.29	0.24	Proportion that have shared equipment in last month: estimate and 95% confidence interval limits from study of Odessa IDUs (n=600) conducted from 2004-07 (8).
7	c_low	c_1	Number of needle-sharing partners in last year, for those that share rarely.	12.00	Uniform	1	12	-99	Between once per year and once per month.
8	c_high	c_2	Number of needle-sharing partners in last year, for those that share often.	107.00	Triangle	50	163	107	Based on number of times shared needles in last month (among those who shared in last month) was 8.9 (4.3-13.6). (8)
9	Epsi_IDU	ε^{idu}	Degree of like-with-like sharing of needles between IDUs.	0.60	Uniform	0.3	0.9	-99	Limited studies suggest weak assortative mixing (27).
10	PrCleaned	δ^{idu}	Fraction of shared needles that are cleaned before re-use.	0.77	Triangle	0.654	0.878	0.766	Estimate and 95% confidence interval limits from study of Odessa IDUs (n=600) conducted from 2004-07 (8).
11	CleaningEfficacy	α^{idu}	Efficacy of cleaning.	0.00	Fixed	-99	-99	-99	Assume that 'cleaning' has no effect in reducing chance of HIV acquisition.
12	Pr_SexRisk_None_Men	$J_{1,1}$	Fraction of male IDU that never have sex.	0.23	Triangle	0.192	0.273	0.233	Estimate and 95% confidence interval

									limits for fraction of men who did not have sex in last 30 days (8).
13	Pr_SexRisk_High_Men	$J_{1,3}/(J_{1,2}+J_{1,3})$	Fraction of male IDU that have sex, that have "many" partners.	0.37	Triangle	0.316	0.421	0.368	Estimate and 95% confidence interval limits of fraction of men reporting more than 1 partner in last 30 days (By Design - "Many" partners corresponds to upper 30th percentile of number of sexual partners in last 30 days) (8).
14	Pr_SexRisk_None_Women	$J_{2,1}$	Fraction of female IDU that never have sex.	0.27	Triangle	0.208	0.34	0.274	Estimate and 95% confidence interval limits of fraction of women who didn't have sex in last 30 days (8).
15	Pr_SexRisk_High_Women	$J_{2,3}/(J_{2,2}+J_{2,3})$	Fraction of female IDU that have sex, that have "many" partners.	0.23	Triangle	0.115	0.301	0.228	By Design - "Many" partners corresponds to upper 30th percentile of number of sexual partners in last 30 days (8).
16	PrMenIDU_MSM	$(K_3+K_4)/(K_1+K_3+K_4$	Fraction of IDU men that have sex with men only or men and women.	0.01	Triangle	0.003	0.0258	0.0144	Reported sexual orientatio as 'gay' or 'bisexual'. (8).
17	Pr_SexRisk_High_MSM	$J_{3,3}=J_{4,3}$	Fraction of MSM that have "many" partners	0.99	Triangle	0.398	0.99	0.99	By Design - "Many" partners corresponds to upper 30th percentile of number

									of sexual partners in last 30 days (8).
18	d_low_Men	$d_{1,2}$	Number of sexual partners per year for men that have "few" partners.	2.78	Triangle	1	6	2.78	Imputed from observation of Mean # of sexual partners in past month for ALL men equal to 1.603 (1.386 - 1.820) . (8)
19	d_high_Men	$d_{1,3}$	Number of sexual partners per year for men that have "many" partners.	47.50	Triangle	40.6	54.3	47.5	Based on mean number of sexual partners in last month for men with "many" sexual partners of 3.958 (3.387 - 4.529) (8).
20	d_low_Women	$d_{2,2}$	Number of sexual partners per year for women that have "few" partners.	2.40	Triangle	1	6	2.40	Imputed from observation of Mean # of sexual partners in past month for ALL women equal to 1.640 (0.973 - 2.307). (8) (Min 1 partner per year, by definition; Maxium set arbitrarily).
21	d_high_Women	$d_{2,3}$	Number of sexual partners per year for women that have "many" partners.	78.20	Triangle	34.1	122.3	78.2	Based on mean number of sexual partners in last month for women with "many" sexual partners of 6.517 (2.840 - 10.195) (8).
22	d_low_MSM	$d_{3,2} = d_{4,2}$	Number of sexual partners per year for MSM that have "few" partners.	2.78	Triangle	1	6	2.78	(Very few men in this category in the data; assume follows same

									distribution as men who have sex with only women).
23	d_high_MSM	$d_{3,3} = d_{4,3}$	Number of sexual partners per year for MSM that have "many" partners.	63.00	Triangle	5.6	131.6	63	Based on mean # of sexual partners in last month for gay and bisexual men with "many" sexual partners of 5.250 (0.469 - 10.969) (8).
24	Epsi_Sex	ε^{sex}	Degree of like-with-like formation of sexual partnerships.	0.60	Uniform	0.3	0.9	-99	Limited studies suggest weak assortative mixing (27).
25	PrMSMSexWithWomen	η	Fraction of MSM that also have sex with women.	0.50	Triangle	0.09	0.9	0.5	Fraction of bisexual men among bisexual and gay men (8).
26	PtrsAreIDU_low	υ_2	Fraction of IDU's sex partners that are also IDUs (for those with "few" partners).	0.58	Triangle	0.526	0.638	0.582	Fraction of IDUs sex partners that were also IDUs in past month among IDUs with "few" partners (8).
27	PtrsAreIDU_high	υ_3	Fraction of IDU's sex partners that are also IDUs (for those with "many" partners).	0.38	Triangle	0.311	0.441	0.376	Fraction of IDU sex partners among IDUs with "many" sex partners (8).
28	theta	θ	Extent to which partnership formation is determined by men.	0.5	Uniform	0.30	0.70	-99	Cannot be directly estimated from data but shown to have potentially important influence of epidemic spread (28).

29	RateOfSexActs_lowlow	$w_{2,2}$	Number of sex acts per partnership per year in partnerships between those that have “few” partnerships.	56.00	Uniform	16	96	-99	Based on approx 1-3 sex acts per week in regular for 4-8 months partnerships (ref).
30	RateOfSexActs_ highlow	$w_{3,3}$	Number of sex acts per partnership per year in partnerships between those have “few” partnerships and those that have “many” partnerships.	56.00	Uniform	16	96	-99	Based on approx 1-3 sex acts per week in regular for 4-8 months partnerships.
31	RateOfSexActs_highhigh	$w_{3,3}$	Number of sex acts per partnership per year in partnerships between those that have “many” partnerships.	3.00	Uniform	1	5	-99	Based on 1-5 sex acts in total in short duration sexual partnerships and in commercial sex.
32	PrCondomUseMF_low	$\delta^{sex}_{1,2,2,2} = \delta^{sex}_{2,1,2,2} = \delta^{sex}_{3,2,2,2} = \delta^{sex}_{2,3,2,2}$	Fraction of sex acts condom used in sex between a man and a woman who each have “few” partnerships.	0.35	Triangle	0.298	0.404	0.351	Fraction of protected vaginal/anal sex acts in last 30 days among heterosexuals who have "few" partners (8).
33	PrCondomUseMF_high	$\delta^{sex}_{1,2,3,j'} = \delta^{sex}_{1,2,2,3} = \delta^{sex}_{2,1,3,j'} = \delta^{sex}_{2,1,2,3}$	Fraction of sex acts condom used in sex between a man and a woman and either or both have “many” partnerships.	0.65	Triangle	0.575	0.721	0.648	Fraction of protected vag/anal sex acts in last 30 days among heterosexuals who have "many" partners (8).
34	PrCondomUseMM_low	$\delta^{sex}_{3,3,2,2} = \delta^{sex}_{3,4,2,2} = \delta^{sex}_{4,3,2,2} = \delta^{sex}_{4,4,2,2}$	Fraction of sex acts condom used in sex between two men and both have “few” partnerships.	0.35	Triangle	0.298	0.404	0.351	Assume distributions for male-female sex.
35	PrCondomUseMM_high	$\delta^{sex}_{3,3,3,j'} = \delta^{sex}_{3,4,3,j'} = \delta^{sex}_{4,3,3,j'} = \delta^{sex}_{4,4,3,j'} = \delta^{sex}_{3,3,2,3'} = \delta^{sex}_{3,4,2,3} = \delta^{sex}_{4,3,2,3} = \delta^{sex}_{4,4,2,3}$	Fraction of sex acts condom used in sex between two men and either or both have “many” partnerships.	0.65	Triangle	0.575	0.721	0.648	Assume distributionas for male-female sex.
36	CondomEfficacy	α^{sex}	Efficacy of condoms (as used).	0.78	Uniform	0.60	0.95	-99	Range from lowest estimate in pooled meta-analysis to highest estimate for perfectly consistent use. (29) Mean is mid-point of range.

37	Beta0_Sex	β_0^{sex}	Average transmission rate of HIV per sex act (in latent infection phase).	0.0038	Log-Normal	-5.573	4.558	-99	Distribution chosen to coincide with point estimate and 95% confidence intervals of meta-analysis of rates of HIV transmission ([95% CI 0.0013-0.0110]) (17).
38	Beta0_IDU	β_0^{idu}	Average transmission rate of HIV per needle-sharing act (in latent infection phase).	0.0085	Uniform	0.0029	0.0141	-99	(23)

Table S2: Parameters for used in model "fitting" for Odessa.

Distribution shapes (and parameterisation) are as follows: *Uniform (*"a" is lower limit; "b" is upper limit); *Triangle (*"a" is lower limit; "b" is upper limit; "c" is mode); *Normal (*"a" is mean; "b" is standard deviation) and Log-*Normal (*"a" is mean; "b" is standard deviation). Note that *-99* is a dummy for "*N/A*".

KARACHI, PAKISTAN					Distribution of prior				
Parameter Number	**Parameter Name**	**Symbol**	**Description**	**Estimate**	**Shape**	**"a"**	**"b"**	**"c"**	**Comments**
1	IDUPop	N_0	Number of IDU.	9000	Triangle	7200	10400	9000	HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007.
2	MortRate	M	Mortality rate of IDU.	0.01	Fixed	-99	-99	-99	1% per year for HIV-IDU (30).
3	DurIDU	L	Mean duration (years) spent as IDU.	9.7	Uniform	4.4	15	-99	Upper limit based on average time since first injection: 4.4 years in 2003 (31) ;Upper limit based on 13.4% having started to inject within two years (32). Estimate is mid-point between these two limits.
4	Pr_IDU_IsMen	$K_1 + K_2 + K_3$	Fraction of IDU that are men.	0.975	Uniform	0.95	1	-99	All literature review for Karachi suggests more than 95% of IDU are men.
5	Pr_IDURisk_None	I_1	Fraction of IDU that never share needles.	0.205	Triangle	0.06	0.82	0.205	Compliment of the fraction of IDU in Karachi reporting "ever" shared ((31) and HIV Second

									Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007.
6	Pr_IDURisk_High	$I_3/\left(I_2+I_3\right)$	Fraction of IDU that ever share needles, that do so often.	0.226	Triangle	0.187	1	0.226	Fraction of IDUs in Karachi that shared, that shared at "last" injection(32) . Range from minimum and maximum fractions reporting sharing in last week (any city in Pakistan) from literature review.
7	c_low	c_1	Number of needle-sharing partners in last year, for those that share rarely.	27	Uniform	2	52	-99	No direct data. Values imply rate of between once every six months and once a week.
8	c_high	c_2	Number of needle-sharing partners in last year, for those that share often.	104	Uniform	52	156	-99	No direct data. Values imply rate of between once a week and three times a week.
9	Epsi_IDU	ε^{idu}	Degree of like-with-like sharing of needles between IDUs.	0.6	Uniform	0.3	0.9	-99	Limited studies suggest weak assortative mixing (27).
10	PrCleaned	δ^{idu}	Fraction of shared needles that are cleaned before re-use.	0.946	Triangle	0.01	0.847	0.793	In Karachi IDUs in 2004, 94.6% cleaned their syringe at last injection (32), but

									the method of cleaning was not given.
11	CleaningEfficacy	α^{idu}	Efficacy of cleaning.	0.00	Fixed	-99	-99	-99	Assume that 'cleaning' has no effect in reducing chance of HIV acquisition.
12	Pr_SexRisk_None_Men	$J_{1,1}$	Fraction of male IDU that never have sex.	0.16	Triangle	0.10	0.25	0.16	16% of male IDUs in a multi-site surveillance study in Pakistan had never had sex in 2006 (HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007).
13	Pr_SexRisk_High_Men	$J_{1,3}/\left(J_{1,2}+J_{1,3}\right)$	Fraction of male IDU that have sex, that have "many" partners.	0.24	Triangle	0.1	0.5	0.24	24% report having sex with female sex worker in the last months; min and max are lowest and highest for IDUs in other cities in Pakistan (HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007).

14	Pr_SexRisk_None_Women	$J_{2,1}$	Fraction of female IDU that never have sex.	0.05	Fixed	-99	-99	-99	Assume most women sexually active.
15	Pr_SexRisk_High_Women	$J_{2,3}/(J_{2,2}+J_{2,3})$	Fraction of female IDU that have sex, that have "many" partners.	0.98	Fixed	-99	-99	**-99**	In 2006, estimate of number of FSWs in Karachi was 13,150, of whom 0.7%-3.0% injected drugs - equivalent to 5% of IDU population (HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007).
16	PrMenIDU_MSM	$(K_3+K_4)/(K_1+K_3+K_4$	Fraction of IDU men that have sex with men only or men and women.	0.41	Triangle	0.07	0.5	0.41	41.2% of male IDUs in Karachi had sex with male sex workers or hijras in last 6 month (32). Range is min and max among male IDU reporting sex with men in any Pakistan city (33) (refs).
17	Pr_SexRisk_High_MSM	$J_{3,3}=J_{4,3}$	Fraction of MSM that have "many" partners	0.24	Triangle	0.1	0.5	0.24	Assume same prior for risk distribution as for other men.
18	d_low_Men	$d_{1,2}$	Number of sexual partners per year for men that have "few" partners.	0.3	Uniform	0.1	0.5	-99	Range is from 1 partners for 10 years to partners for 2 year (corresponds to men who do not buy sex).

19	d_high_Men	$d_{1,3}$	Number of sexual partners per year for men that have "many" partners.	13	Uniform	2	24	-99	Range is from 2 partners per year to two partner per month (corresponds to men who buy sex).
20	d_low_Women	$d_{2,2}$	Number of sexual partners per year for women that have "few" partners.	0.3	Uniform	0.1	0.5	-99	Range is from 1 partner for 10 years to partners for 2 year (corresponds to women).
21	d_high_Women	$d_{2,3}$	Number of sexual partners per year for women that have "many" partners.	348	Triangle	200	500	348	Corresponds to women that sell sex; and female sex workers from Karachi reported 29 clients/mo in 2007m equivalent to 348 per year (HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007.)
22	d_low_MSM	$d_{3,2} = d_{4,2}$	Number of sexual partners per year for MSM that have "few" partners.	0.3	Uniform	0.1	0.5	-99	Range is from 1 partners for 10 years to partners for 2 year (corresponds to married men).
23	d_high_MSM	$d_{3,3} = d_{4,3}$	Number of sexual partners per year for MSM that have "many" partners.	300	Uniform	100	400	-99	Male sex workers and Hijras in Karachi had 25 male sex partners/mo, corresponding to 300 per year (HIV Second

									Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007).
24	Epsi_Sex	ε^{sex}	Degree of like-with-like formation of sexual partnerships.	0.6	Uniform	0.3	0.9	-99	Limited studies suggest weak assortative mixing (27).
25	PrMSMSexWithWomen	η	Fraction of MSM that also have sex with women.	0.75	Uniform	0.5	0.99	-99	Between half and all of those have sex with men also have sex with women.
26	PtrsAreIDU_low	υ_2	Fraction of IDU's sex partners that are also IDUs (for those with "few" partners).	0.05	Uniform	0.01	0.09	-99	Assumed to be low given small numbers of women IDU, frequency of male IDU reporting sex with sex worker, and low proportion of sex workers than inject drugs.
27	PtrsAreIDU_high	υ_3	Fraction of IDU's sex partners that are also IDUs (for those with "many" partners).	0.05	Uniform	0.01	0.09	-99	Assumed to be low given small numbers of women IDU, frequency of male IDU reporting sex with sex worker, and low proportion of sex workers than inject drugs.
28	theta	θ	Extent to which partnership formation is determined by men.	0.05	Uniform	0.3	0.7	-99	Cannot be directly estimated from data

									but shown to have potentially important influence of epidemic spread [25].
29	RateOfSexActs_lowlow	$w_{2,2}$	Number of sex acts per partnership per year in partnerships between those that have “few” partnerships.	150	Uniform	100	200	-99	Based on approx 2-4 sex acts per week in regular partnerships.
30	RateOfSexActs_ highlow	$w_{3,3}$	Number of sex acts per partnership per year in partnerships between those have “few” partnerships and those that have “many” partnerships.	10	Uniform	5	15	-99	Based on 5-15 sex acts in total in short duration sexual partnerships and at commercial sex.
31	RateOfSexActs_highhigh	$w_{3,3}$	Number of sex acts per partnership per year in partnerships between those that have “many” partnerships.	2	Uniform	1	3	-99	Based on 1-3 sex acts in total in short duration sexual partnerships and at commercial sex.
32	PrCondomUseMF_low	$\delta^{sex}_{1,2,2,2} = \delta^{sex}_{2,1,2,2} = \delta^{sex}_{3,2,2,2} = \delta^{sex}_{2,3,2,2}$	Fraction of sex acts condom used in sex between a man and a woman who each have “few” partnerships.	0.10	Uniform	0.00	0.2	-99	Assumed to be low in long-term relationships. 33% of IDUs in Karachi in 2006 report 'ever' using condoms (HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007).
33	PrCondomUseMF_high	$\delta^{sex}_{1,2,3,j'} = \delta^{sex}_{1,2,2,3} = \delta^{sex}_{2,1,3,j'} = \delta^{sex}_{2,1,2,3}$	Fraction of sex acts condom used in sex between a man and a woman and either or both have “many” partnerships.	0.220	Triangle	0.000	0.530	0.220	22% of IDU used condom at last sex with sex worker in Karachi (32); 21% of

									IDUs used condoms in commercial sex transactions in multi-city surveillance in 2007; 44% of FSWs in Karachi consistently used condoms in 2006. Max based on range of 'ever condom use with sex worker' in any Pakistan city.
34	PrCondomUseMM_low	$\delta^{sex}_{3,3,2,2} = \delta^{sex}_{3,4,2,2} = \delta^{sex}_{4,3,2,2} = \delta^{sex}_{4,4,2,2}$	Fraction of sex acts condom used in sex between two men and both have “few” partnerships.	0.030	Triangle	0.000	0.080	0.030	3% of MSM IDU in Karachi report condom use in sex with men. Range is min and max and men IDU reporting condom use in male-male sex in any Pakistan city. (HIV Second Generation Surveillance in Pakistan; National Report Round II; 2006-2007; National AIDS Control Program 2007; andHIV Second Generation Surveillance in Pakistan)
35	PrCondomUseMM_high	$\delta^{sex}_{3,3,3,j'} = \delta^{sex}_{3,4,3,j'} = \delta^{sex}_{4,3,3,j'} = \delta^{sex}_{4,4,3,j'} = \delta^{sex}_{3,3,2,3'} = \delta^{sex}_{3,4,2,3} = \delta^{sex}_{4,3,2,3} = \delta^{sex}_{4,4,2,3}$	Fraction of sex acts condom used in sex between two men and either or both have “many” partnerships.	0.110	Uniform	0.00	0.220	-99.000	In 2006 in Karachi, 22% of male sex workers report consistent condom use with clients (HIV Second Generation

									Surveillance in Pakistan; National Report Round III; 2006-2007) which is interpreted as an upper bound on the true level of condom use.
36	CondomEfficacy	α^{sex}	Efficacy of condoms (as used).	0.78	Uniform	0.60	0.95	-99	Range from lowest estimate in pooled meta-analysis to highest estimate for perfectly consistent use. (29) Estimate is mid-point of range.
37	Beta0_Sex	β_0^{sex}	Average transmission rate of HIV per sex act (in latent infection phase).	0.0038	Log-Normal	-5.573	4.558	-99	Distribution chosen to coincide with point estimate and 95% confidence intervals of meta-analysis of rates of HIV transmission ([95% CI 0.0013-0.0110]) (17).
38	Beta0_IDU	β_0^{idu}	Average transmission rate of HIV per needle-sharing act (in latent infection phase).	0.0085	Uniform	0.0029	0.0141	-99	Based on literature review (23).

Table S3: Parameters for used in model “fitting” for Karachi.

Distribution shapes (and parameterisation) are as follows: *Uniform (*"a" is lower limit; "b" is upper limit); *Triangle (*"a" is lower limit; "b" is upper limit; "c" is mode); *Normal (*"a" is mean; "b" is standard deviation) and Log-*Normal (*"a" is mean; "b" is standard deviation). Note that *-99* is a dummy for “*N/A*”.

Year of observation	(Effective) Sample Size	HIV prevalence estimate	Source
2004	132	54.6%	(8)
2005	269	41.3%	(34)
2005	314	50.0%	(8)
2006	554	51.6%	(8)
2007	594	52.5%	(8)
2008	11	63.6%	*(35)*
2008	400	37.5%	*(36)*

Table S4: Prevalence data for Odessa model.

Year of observation	(Effective) Sample Size	HIV prevalence estimate	Source
1996	242	0.4%	(37)
2003	242	23.0%	(32)
2003	242	26.3%	(31)
2005	242	26.5%	(38)
2006	399	30.1%	(39)
2008	406	23.1%	(40)

Table S5: Prevalence data for Karachi model.

Methods for Nairobi Modelling

The modelling for the HIV transmission among IDU in Nairobi is complicated by the need to incorporate the high HIV prevalence rates among other populations, such as non-IDU sex workers and the general population, whilst a detailed model representation of the IDU population is prevented by the limited current availability of data on IDU population size and HIV prevalence among IDUs (We note, however, that from mid-2010, substantially more data will be available from a large survey). For these reasons, a different and simplified model of HIV transmission within and between risk groups was developed. This model built on the UNAIDS 'Modes of Transmission Model' (MoT) (41, 42), which has recently been applied to Kenya and Nairobi (43). This model examines the HIV epidemic in a particular population (in this case Nairobi) at one instant in time and, based on the HIV prevalence in discrete risk groups and estimated patterns of risk behaviour, projects the number of HIV infection, by risk-group, over the next year. In the MoT model, the risk groups include IDU, Men who have sex with Men, Female commercial sex workers, those having casual heterosexual partnerships and those at no risk of HIV infection. In Nairobi, it was estimated that approximately 5% of new infection currently arise among the IDU population (43).

The model was developed to incorporate more detail about the IDU population. The IDU population was divided into sub-groups of IDU Men, IDU Women, IDU Men who have sex with men and IDU Women who sell sex. IDU in the model were thus exposed to a risk of HIV infection via sexual contact in addition to the risk of HIV infection via exposure to contaminated injecting equipment. It was assumed that the risk of transmission IDU-MSM through sex with men was the same as for other MSM; that the risk of transmission to IDU-CSW through sex with client was the same as for other CSW; and that the risk of transmission to other IDU through sex was the same as for others having casual heterosexual partnerships. It was assumed that IDU-MSM mixed randomly with non-IDU MSM; that IDU-CSW mix randomly with clients; and that IDU men and women mix randomly with non-IDU women and men, respectively. A 'pattern of contact' parameter was introduced that allow the rate of HIV transmission to IDU to represent, at one extreme, IDU mixing "randomly" (where at each injection, the individual IDU uses a syringe that could have previously used by any other IDU) or, at the other extreme, IDU forming "stable injecting partnerships" (where syringes are only shared with one partner). Changes in prevalence over time were reproduced by assuming a mean survival time after HIV infection of 10.0 years, and the IDU population size was allowed to grow at a fixed rate, with the assumption that all new IDU were uninfected.

To ensure consistency of the model results with other epidemiological information, the estimated total number of new infections among the non-IDU population per year in Nairobi in the model with no further intervention was constrained to be equal with HIV incidence rate estimated in the UNAIDS (Spectrum model (44, 45)) estimates 2007.

The uncertainty in the model projections is approximated using a Monte Carlo scheme, allowing parameters relating to IDU population size, prevalence and behaviour to independently vary over a uniform distribution (with bounds specified below).

The impact of OST and NEP were incorporated by allowing, for a proportion of IDU population given by the intervention 'coverage', the rate of exposure to non-sterile syringes to be reduced by the assumed efficacy of that intervention (see '*Assumed Efficacy of OST/NEP Interventions*' above). The impact of ART was incorporated by reducing the infectiousness of a proportion of the HIV-infected IDU population expected to be in need of treatment. This implies ART being required for individuals with a CD4 cell count of less than 350 cells per microliter of peripheral blood. With analogy to the models in Odessa and Karachi, this amount to assuming that 40% of all HIV-infected individual are in need of treatment (20), and that treatment reduces infectiousness by 92%, on average (24).

Table S6 lists the parameter values used for the modelling projections. Values for other model behaviour parameters were based on Kenya MoT project, where parameters were evaluated through literature reviews and with expert opinions, and around which a broad consensus was developed (43). Parameters specifying HIV transmission rates are the same as the same as used in the other models (Table S1).

Parameter	Value or Range	Source
Number of IDU	3000-5000	*UNODC Regional Office for Eastern Africa.*
IDU population annual growth rate.	0%-4%	*UNODC Regional Office for Eastern Africa*
HIV prevalence among IDU in 2010	33% - 50%	Lower-bound is self-reported HIV test result in Nairobi Outreach Services Trust UNODC Report on Contacts, Average Jan-Oct 2000 (46); Upper bound is empirical observation of HIV prevalence among IDU in Mombasa in 2004 (47).
Proportion of IDU: *IDU-Female* *IDU-Female Sex Worker* *IDU-Male* *IDU-Msm* *IDU-Male That Buy Sex*	 7.00% 12.00% 65.61% 7.29% 8.10%	*Nairobi Outreach Services Trust UNODC Report on Contacts 2009*
Frequency of Injecting with non-sterile equipment per week	3.6 (1-6)	Mean and 95% interval of reported numbers of injections per week with 'shared' syringes/needles, among IDU contact in Nairobi (46).

Pattern of Contact Parameter	0-0.5	Broad range represent substantial uncertainty in mixing pattern, although it is assumed that mixing is more likely to be based around sets of injecting partnerships than fully random mixing. (0 indicates stable injecting partnerships; 1 indicates random mixing.)
Baseline Coverage of OST in 2010	0	*UNODC Regional Office for Eastern Africa.*
Baseline Coverage of NEP in 2010	0	*UNODC Regional Office for Eastern Africa*
Fraction of individuals expected to be able to access ART, when required, in 2010.	30%	*UNODC Regional Office for Eastern Africa*

Table S6: Parameter value for Nairobi IDU model.

Summary Statistics: Studies of HIV Risk Factors, Correlates and Determinants among IDU Populations: Summary Statistics from 2000-2009

		1999-2001		2002-2004		2005-2007		2008-2009		All Years		P-value [3]
		N		N		N		N		N		
Total		14	100·0%	22	100·0%	36	100·0%	22	100·0%	94	100·0%	0·168
Prospective or Panel Study		6	42·9%	12	54·5%	14	38·9%	5	22·7%	37	39·4%	0·496
Conducted in low/middle income country [1]		3	21·4%	7	31·8%	14	38·9%	11	50·0%	35	37·2%	0·018
Country with HIV prevalence among IDUs = 20% [2]		4	28·6%	7	31·8%	12	33·3%	4	18·2%	27	28·7%	0·32
Aimed to study risk environment		6	42·9%	1	4·5%	12	30·6%	6	27·3%	25	26·5%	0·336
Identified >= one risk environment factor		12	85·7%	18	81·8%	32	88·9%	19	86·4%	81	86·2%	0·192
	Micro-physical	4	28·6%	9	40·9%	19	52·8%	10	45·5%	42	44·7%	0·068
	Micro-social	7	50·0%	12	54·5%	16	44·4%	7	31·8%	42	44·7%	0·979
	Micro-economic	4	28·6%	3	13·6%	4	11·1%	4	18·2%	15	16·0%	0·968
	Micro-policy	0	0·0%	2	9·1%	5	13·9%	4	18·2%	11	11·7%	0·034
	Macro-physical	1	7·1%	1	4·5%	2	5·6%	1	4·5%	5	5·3%	0·31
	Macro-social	2	14·3%	4	18·2%	11	30·6%	7	31·8%	24	25·5%	0·031
	Macro-economic	0	0·0%	0	0·0%	1	2·8%	0	0·0%	1	1·1%	0·631
	Macro-policy	2	14·3%	0	0·0%	0	0·0%	1	4·5%	3	3·2%	0·811
Identified >= one risk environment factor excluding sex/race		11	78·6%	16	72·7%	29	80·6%	18	81·8%	74	78·7%	0·164
Identified >= one endogenous host factor		11	78·6%	16	72·7%	25	69·4%	13	59·1%	65	69·1%	0·528
Identified >= one endogenous biologic factor		1	7·1%	2	9·1%	4	11·1%	7	31·8%	14	14·9%	0·018
Identified one endogenous host, one endogenous biologic, and one risk environment factor		1	7·1%	2	9·1%	2	5·6%	3	13·6%	8	8·5%	0·43
Identified at least one micro level factor (As proportion of papers that identified at least one risk environment factor)		9	75·0%	16	88·9%	28	87·5%	17	89·5%	70	86·4%	0·126
Identified at least one macro level factor		4	33·3%	5	27·8%	13	40·6%	8	42·1%	30	37·0%	0·094
Macro-level Risk environment variables identified		5	13·2%	5	13·2%	16	42·1%	12	31·6%	38	100·0%	0·018
	Physical	1	2·6%	1	2·6%	2	5·3%	1	2·6%	5	13·2%	0·314
	Social	2	5·3%	4	10·5%	13	34·2%	10	26·3%	29	76·3%	0·015
	Economic	0	0·0%	0	0·0%	1	2·6%	0	0·0%	1	2·6%	0·631
	Policy	2	5·3%	0	0·0%	0	0·0%	1	2·6%	3	7·9%	0·811
Micro-level Risk environment variables identified		25	16·9%	36	24·3%	52	35·1%	34	23·0%	148	100·0%	0·415
	Physical	7	4·7%	14	9·5%	22	14·9%	11	7·4%	54	36·5%	0·399
	Social	14	9·5%	17	11·5%	19	12·8%	14	9·5%	64	43·2%	0·914
	Economic	4	2·7%	3	2·0%	5	3·4%	5	3·4%	17	11·5%	0·66
	Policy	0	0·0%	2	1·4%	7	4·7%	4	2·7%	13	8·8%	0·035

[1] Income level groups follow World Bank categories.
<<http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,contentMDK:20421402~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html>
[2] Countries with HIV prevalence among IDUs ≥ 20% according to Mathers et al (reference 1 in paper) include Argentina, Brazil, Burma, Cambodia, China, Estonia, Kenya, Libya, Nepal, Russia, Spain, Thailand, Ukraine, Vietnam.
[3] P-values are for the coefficient in a regression of the number of papers in each category on year.

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