Supplementary Material for "Needle-syringe programs are cost-effective in Eastern Europe and Central Asia: costing, data synthesis, modeling and economics for nine case study countries"

Description of mathematical model

A mathematical model was developed to estimate HIV and HCV incidence and other disease outcomes. The model tracks the population of injecting drug users (PWID), and it was formulated to describe the change in the number of people in different disease states over time. The model tracks the entry of new injectors into the uninfected population and those who die, rates differentiated by health state, over time.

A schematic diagram of compartments in the HIV and HCV transmission model for PWID is presented in Figure S1. The change in the number of people in each compartment was tracked mathematically by formulating a system of ordinary differential equations. Twenty compartments represent PWID who are infected with HIV: CD4+ T cell levels (>500 cells per μl, 350-500 cells per μl, 200-350 cells per μl, and <200 cells per μl) for both diagnosed and undiagnosed; then HIV diagnosed individuals may initiate antiretroviral therapy for first-line treatment; for those who failed treatment may receive second-line treatment; a twenty-first compartment represents uninfected PWID. The description of health states are shown in Table S1. Twenty-one compartments represent PWID who are infected with HCV: in acute stage, fibrosis stages F0, F1, F2, F3, and F4, whether they are diagnosed, undiagnosed or receiving treatment. People infected with HCV who have advanced fibrosis can progress to clinical outcomes of liver failure, hepatocellular carcinoma, or may receive a liver transplant. It is assumed that individuals who progress to these three clinical outcomes no longer receive HCV treatment due to the severity of their health status.

Figure S1: Schematic diagram of HIV and HCV disease progression among PWID in Australia. Each arrow represents the change in the number of people in the population moving from one health compartment state to the other compartment.

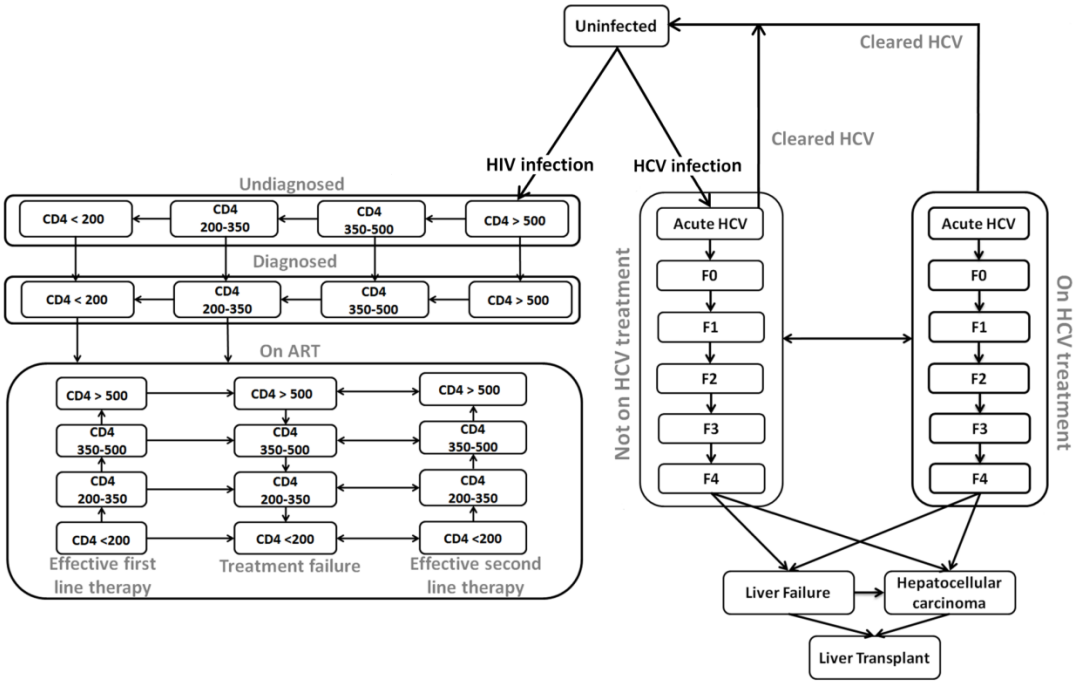


Table S1: Number of compartments in HIV/HCV model

HIV	HCV
1. Uninfected HIV	1. Uninfected HCV
2-5. Infected, Undiagnosed (CD4>500, CD4 350-500, CD4 200-350, CD4<200)	2-7. Infected, Undiagnosed (Acute, F0-F4)
6-9. Infected, Diagnosed (CD4>500, CD4 350-500, CD4 200-350, CD4<200)	8-13. Infected, Diagnosed (Acute, F0-F4)
10-13. Infected, 1stline ART (CD4>500, CD4 350-500, CD4 200-350, CD4<200)	14-19. Infected, Treatment (Acute, F0-F4)
14-17. Infected, Failure of ART (CD4>500, CD4 350-500, CD4 200-350, CD4<200)	20-22. Liver failure, hepatocellular carcinoma, liver Transplant
18-21. Infected, 2ndline ART (CD4>500, CD4 350-500, CD4 200-350, CD4<200)	

One ordinary differential equation (ODE) was developed to describe the change in the number of people in each of these compartmental health states over time, for 43 ODEs in total. The rate of change in the numbers of people in each compartment depends on the net effect of rates of people entering the health state and the rate of leaving the health state. Each ODE was mathematically described based on standard translation from the schematic diagram of the model presented in Figure S1 [1] (with the addition of rates of initiation of injecting and leaving the population (background death/migration/cessation of injecting, drug-related death, health state-specific death)). For example, the ODE representing the rate of change in the number of people uninfected with HIV can be written as following:

$$\underbrace{\frac{dS}{dt}}_{\text{Change in uninfecteds}} = \underbrace{\pi}_{\text{Entry into population}} - \left(\underbrace{\lambda}_{\text{Force of HIV infection}} + \underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} \right) S$$

where S is the number of uninfected active PWID, π is the annual number of people who commence injecting drugs, μ is the mortality rate among general population, μ_D is the drug-related death rate, and λ is the 'force of infection' or per-capita rate at which susceptible PWID acquire infection. The complete lists of model parameters for HIV and HCV transmission and disease progression are in Table S9 and S10.

The force of infection is dependent on other health states (namely, numbers of people in the infected health states). To calculate the force of infection, we assume that each PWID injects an average of n times per year and denote the receptive syringe sharing rate (RSS) as s, and the prevalence in the population as *P(t)*. The probability of infection from a contaminated syringe per use is denoted by β.

We assume that syringe cleaning has effectiveness ε_c and cleaning occurs in p_c proportion of shared injections. Given these definitions, the force of infections is given mathematically by:

$$\lambda = (1 - (1 - (1 - \ p_c\varepsilon_c)\beta)^{ns})P(t).$$

The model is calibrated to the data provided using a mixture of optimization and force-fitting. A force-fitting algorithm assumes an initial 100% accuracy in the epidemiological data and derives the distribution of behavioral data that would result in the epidemic trend. This algorithm preferentially gives greater weighting to epidemiological and biological indicators (e.g. prevalence and diagnoses) over behavioral indicators (e.g. self-reported drug usage) during the optimization process. This assumption is based on the fact that epideimological and biological indicators are derived from medical tests (e.g. screening and confirmation tests for HIV infection). These indicators are considered to be more reliable than self-reported behaviors that are subjected to recall bias and socially desirable responses. In contrast to a conventional fitting strategy that predicts epidemic trends based on behavioral patterns, force-fitting determines the likelihood of risk behaviors based on reported epidemiological/biological indicators. By comparing the derived distribution to the actual behavioral data, the fit to the epidemiological indicators is then adjusted to accommodate the discrepancies between the distributions. The adjustment is then repeated until the scenario with the least sum of weighted errors between model-simulated results and the actual data is reached within the given uncertainty bounds of both epidemiological and behavioral indicators. In this manner, the model is force-fitted to population size, HIV diagnoses, AIDS diagnoses, and number of people on HIV/HCV treatment. This method alters the source parameters to ensure that the model will match the given epidemiological data. Once these epidemiological data have been force-fitted, the model employs a trust-region-reflective algorithm on the biological model parameters (e.g., disease progression rates) to obtain the best fit (in the least square sense) to prevalence data. The trust-region reflective algorithm [2] is a gradient-descent algorithm that calculates the Hessian matrix (i.e., the second derivatives) of the function to be optimized in order to determine the step size (the “trust region”) for the current iteration. It is a generalization of the Levenberg-Marquardt method [3] that allows hard limits on parameter values. The algorithm was invoked via the lsqnonlin function from the Optimization Toolbox in Matlab 2012a (The Mathworks). In some cases, the force-fitting and trust-region-reflective algorithms were unable to find a reasonable fit to the available data; in these cases, parameter value initializations were manually modified and the optimization algorithms were rerun. In all cases where this approach was used, the manually initialized fits had lower mean-squared error and were thus objectively better fits to the data. The optimized parameters thus obtained were used to produce the best-fit estimates presented in the report. Uncertainty estimates, in contrast, were not based on optimized parameter values, but rather by randomly sampling each parameter from within the limits provided in Tables S9 and S10, as described in the main text.

The complete list of ordinary differential equations depicting model in Figure S1 is as follows:

Uninfected IDUs

$$\overbrace{\frac{dS}{dt}}^{\text{Change in uninfecteds}} = \overbrace{\pi}^{\text{Entry into population}} - \left(\overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} \right) S$$

$$+ \overbrace{\gamma_A^M \nu_A^M I_A^{MT}}^{\text{Viral clearance from treatment (acute)}} + \overbrace{\gamma_{F0}^M \nu_F^M I_{F0}^{MT}}^{\text{Viral clearance from treatment (F0)}} + \overbrace{\gamma_{F1}^M \nu_F^M I_{F1}^{MT}}^{\text{Viral clearance from treatment (F1)}} + \overbrace{\gamma_{F2}^M \nu_F^M I_{F2}^{MT}}^{\text{Viral clearance from treatment (F2)}}$$

$$+ \overbrace{\gamma_{F3}^M \nu_F^M I_{F3}^{MT}}^{\text{Viral clearance from treatment (F3)}} + \overbrace{\gamma_{F4}^M \nu_F^M I_{F4}^{MT}}^{\text{Viral clearance from treatment (F4)}} + \overbrace{\psi_M I_A^M}^{\text{Spontaneous viral clearance (acute)}}$$

HCV-infected individuals

$$\overbrace{\frac{dI_A^M}{dt}}^{\text{Change in acute infecteds}} = \overbrace{\lambda_{HCV} S}^{\text{New infections}} + \overbrace{\left(1-\gamma_A^M\right)\nu_A^M I_A^{MT}}^{\text{Cease treatment (acute)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} \right.$$

$$\left. + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\tau_A^M}^{\text{Progress to F0}} + \overbrace{\eta_A}^{\text{Commence treatment (acute)}} \right) I_A^M$$

$$\overbrace{\frac{dI_{F0}^M}{dt}}^{\text{Change in F0 infecteds}} = \overbrace{\tau_A^M I_A^M}^{\text{Progress from acute}} + \overbrace{(1-\gamma_{F0}^M)\nu_F^M I_{F0}^{MT}}^{\text{Cease treatment (F0)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} \right.$$

$$\left. + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\eta_{F0}}^{\text{Commence treatment (F0)}} + \overbrace{\tau_{F0}^M}^{\text{Progress to F1}} \right) I_{F0}^M$$

$$\overbrace{\frac{dI_{F1}^{M}}{dt}}^{\text{Change in F1 infecteds}} = \overbrace{\tau_{F01}^{M} I_{F0}^{M}}^{\text{Progress from F0}} + \overbrace{(1-\gamma_{F1}^{M})\nu_{F}^{M} I_{F1}^{MT}}^{\text{Cease treatment (F1)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\eta_{F1}}^{\text{Commence treatment (F1)}} + \overbrace{\tau_{F1}^{M}}^{\text{Progress to F2}} \right) I_{F1}^{M}$$

$$\overbrace{\frac{dI_{F2}^{M}}{dt}}^{\text{Change in F2 infecteds}} = \overbrace{\tau_{F1}^{M} I_{F1}^{M}}^{\text{Progress from F1}} + \overbrace{(1-\gamma_{F2}^{M})\nu_{F}^{M} I_{F2}^{MT}}^{\text{Cease treatment (F2)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\eta_{F2}}^{\text{Commence treatment (F2)}} + \overbrace{\tau_{F2}^{M}}^{\text{Progress to F3}} \right) I_{F2}^{M}$$

$$\overbrace{\frac{dI_{F3}^{M}}{dt}}^{\text{Change in F3 infecteds}} = \overbrace{\tau_{F2}^{M} I_{F2}^{M}}^{\text{Progress from F2}} + \overbrace{(1-\gamma_{F3}^{M})\nu_{F}^{M} I_{F3}^{MT}}^{\text{Cease treatment (F3)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\eta_{F3}}^{\text{Commence treatment (F3)}} + \overbrace{\tau_{F3}^{M}}^{\text{Progress to F4}} \right) I_{F3}^{M}$$

$$\overbrace{\frac{dI_{F4}^{M}}{dt}}^{\text{Change in F4 infecteds}} = \overbrace{\tau_{F3}^{M} I_{F3}^{M}}^{\text{Progress from F3}} + \overbrace{(1-\gamma_{F4}^{M})\nu_{F}^{M} I_{F4}^{MT}}^{\text{Cease treatment (F4)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{\eta_{F4}}^{\text{Commence treatment (F4)}} + \overbrace{\tau_{F4LF}^{M}}^{\text{Progress to liver failure}} + \overbrace{\tau_{F4HCC}^{M}}^{\text{Progress to HCC}} \right) I_{F4}^{M}$$

$$\overbrace{\frac{dI_A^{MT}}{dt}}^{\text{Change in acute infecteds on treatment}} = \overbrace{\eta_A I_A^M}^{\text{Commenced treatment (acute)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{(1-\gamma_A^M)\nu_A^M}^{\text{Cease treatment (F4)}} + \overbrace{\gamma_A^M \nu_A^M}^{\text{Viral clearance on treatment (acute)}} + \overbrace{\tau_A^{MT}}^{\text{Progress to F0 during treatment}} \right) I_A^{MT}$$

$$\overbrace{\frac{dI_{F0}^{MT}}{dt}}^{\text{Change in F0 infecteds on treatment}} = \overbrace{\tau_A^{MT} I_A^{MT}}^{\text{Progress from acute during treatment}} + \overbrace{\eta_{F0} I_{F0}^M}^{\text{Commenced treatment (F0)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{(1-\gamma_{F0}^M)\nu_F^M}^{\text{Cease treatment (F0)}} + \overbrace{\gamma_{F0}^M \nu_F^M}^{\text{Viral clearance on treatment (F0)}} + \overbrace{\tau_{F0}^{MT}}^{\text{Progress to F1 during treatment}} \right) I_{F0}^{MT}$$

$$\overbrace{\frac{dI_{F1}^{MT}}{dt}}^{\text{Change in F1 infecteds on treatment}} = \overbrace{\tau_{F0}^{MT} I_{F0}^{MT}}^{\text{Progress from F0 during treatment}} + \overbrace{\eta_{F1} I_{F1}^M}^{\text{Commenced treatment (F1)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{(1-\gamma_{F1}^M)\nu_F^M}^{\text{Cease treatment (F1)}} + \overbrace{\gamma_{F1}^M \nu_F^M}^{\text{Viral clearance on treatment (F1)}} + \overbrace{\tau_{F1}^{MT}}^{\text{Progress to F2 during treatment}} \right) I_{F1}^{MT}$$

$$\overbrace{\frac{dI_{F2}^{MT}}{dt}}^{\text{Change in F2 infecteds on treatment}} = \overbrace{\tau_{F1}^{MT} I_{F1}^{MT}}^{\text{Progress from F1 during treatment}} + \overbrace{\eta_{F2} I_{F2}^M}^{\text{Commenced treatment (F2)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{(1-\gamma_{F2}^M)\nu_F^M}^{\text{Cease treatment (F2)}} + \overbrace{\gamma_{F2}^M \nu_F^M}^{\text{Viral clearance on treatment (F2)}} + \overbrace{\tau_{F2}^{MT}}^{\text{Progress to F3 during treatment}} \right) I_{F2}^{MT}$$

$$\overbrace{\frac{dI_{F3}^{MT}}{dt}}^{\text{Change in F3 infecteds on treatment}} = \overbrace{\tau_{F2}^{MT} I_{F2}^{MT}}^{\text{Progress from F2 during treatment}} + \overbrace{\eta_{F3} I_{F3}^{M}}^{\text{Commenced treatment (F3)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{(1-\gamma_{F3}^{M})\nu_F^M}^{\text{Cease treatment (F3)}} + \overbrace{\gamma_{F3}^{M}\nu_F^M}^{\text{Viral clearance on treatment (F3)}} + \overbrace{\tau_{F3}^{MT}}^{\text{Progress to F4 during treatment}} \right) I_{F3}^{MT}$$

$$\overbrace{\frac{dI_{F4}^{MT}}{dt}}^{\text{Change in F4 infecteds on treatment}} = \overbrace{\tau_{F3}^{MT} I_{F3}^{MT}}^{\text{Progress from F3 during treatment}} + \overbrace{\eta_{F4} I_{F4}^{M}}^{\text{Commenced treatment (F4)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\lambda_{HIV}}^{\text{Force of HIV infection}} + \overbrace{(1-\gamma_{F4}^{M})\nu_F^M}^{\text{Cease treatment (F4)}} + \overbrace{\gamma_{F4}^{M}\nu_F^M}^{\text{Viral clearance on treatment (F4)}} \right) I_{F4}^{MT}$$

$$\overbrace{\frac{dI_{LF}^{M}}{dt}}^{\text{Change in liver failure infecteds}} = \overbrace{\tau_{F4LF}^{M} I_{F4}^{M}}^{\text{Progress from F4}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{LF}}^{\text{Liver failure related death}} + \overbrace{\xi_L}^{\text{Leaving population with liver disease}} + \overbrace{\tau_{LFHCC}}^{\text{Progress to HCC}} + \overbrace{\tau_{LFLT}}^{\text{Progress to LT}} \right) I_{LF}^{M}$$

$$\overbrace{\frac{dI_{HCC}^{M}}{dt}}^{\text{Change in HCC infecteds}} = \overbrace{\tau_{F4HCC}^{M} I_{F4}^{M}}^{\text{Progress from F4}} + \overbrace{\tau_{LFHCC}^{M} I_{LF}^{M}}^{\text{Progress from LF}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{HCC}}^{\text{HCC related death}} + \overbrace{\xi_L}^{\text{Leaving population with liver disease}} + \overbrace{\tau_{HCCLT}}^{\text{Progress to LT}} \right) I_{HCC}^{M}$$

$$\overbrace{\frac{dI_{LT}^{M}}{dt}}^{\text{Change in Liver transplants}} = \overbrace{\tau_{LFLT}^{M} I_{LF}^{M}}^{\text{Progress from liver failure}} + \overbrace{\tau_{HCCLT}^{M} I_{HCC}^{M}}^{\text{Progress from HCC}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{LT}}^{\text{Liver transplant related death}} + \overbrace{\xi_L}^{\text{Leaving population with liver disease}} \right) I_{LT}^{M}$$

HIV-infected individuals

$$\overbrace{\frac{dI^{M}_{500}}{dt}}^{\text{Change in infecteds (CD4>500)}} = \overbrace{\lambda_{HIV}S}^{\text{New infections}} + \overbrace{\psi_C I^{A}_{500}}^{\text{Spontaneous HCV clearance (acute coinfecteds)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{500}}^{\text{HIV-related death (CD4>50}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\tau^{M}_{500}}^{\text{Progress to 350<CD4<500}} + \overbrace{\eta^{D}_{500}}^{\text{Commence 1st line treatment(CD4>500, Detectable viral load)}} + \overbrace{\eta^{U}_{500}}^{\text{Commence 1st line treatment(CD4>500, Undetectable viral load)}} \right) I^{M}_{500}$$

$$\overbrace{\frac{dI^{M}_{350\_500}}{dt}}^{\text{Change in infecteds (350<CD4<500)}} = \overbrace{\tau^{M}_{500}I^{M}_{500}}^{\text{Progress from CD4>500}} + \overbrace{\psi_C I^{A}_{350\_500}}^{\text{Spontaneous HCV clearance (acute, 350<CD4<500)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{350\_500}}^{\text{HIV-related death (350<CD4<500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\tau^{M}_{350\_500}}^{\text{Progress to 200<CD4<350}} + \overbrace{\eta^{D}_{350\_500}}^{\text{Commence 1st line treatment (350<CD4<500, Detectable Viral Load)}} + \overbrace{\eta^{U}_{350\_500}}^{\text{Commence 1st line treatment (350<CD4<500, Undetectable Viral Load)}} \right) I^{M}_{350\_500}$$

$$\overbrace{\frac{dI^{M}_{200\_350}}{dt}}^{\text{Change in infecteds (200<CD4<350)}} = \overbrace{\tau^{M}_{350\_500}I^{M}_{350\_500}}^{\text{Progress from 350<CD4<500}} + \overbrace{\psi_C I^{A}_{200\_350}}^{\text{Spontaneous HCV clearance (acute, 200<CD4<350)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200\_350}}^{\text{HIV-related death (200<CD4<350)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\tau^{M}_{200\_350}}^{\text{Progress to CD4<200}} + \overbrace{\eta^{D}_{200\_350}}^{\text{Commence 1st line treatment (200<CD4<350, Detectable Viral Load)}} + \overbrace{\eta^{U}_{200\_350}}^{\text{Commence 1st line treatment (200<CD4<350, Undetectable Viral Load)}} \right) I^{M}_{200\_350}$$

$$\overbrace{\frac{dI^{M}_{200}}{dt}}^{\text{Change in infecteds (CD4<200)}} = \overbrace{\tau^{M}_{200\_350} I^{M}_{200\_350}}^{\text{Progress from 200<CD4<350}} + \overbrace{\psi_C I^{A}_{200}}^{\text{Spontaneous HCV clearance (acute, CD4<200)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200}}^{\text{HIV-related death (CD4<200)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\eta^{D}_{200}}^{\text{Commence 1st line treatment (CD4<200, Detectable Viral Load)}} + \overbrace{\eta^{U}_{200}}^{\text{Commence 1st line treatment (CD4<200, Undetectable Viral Load)}} \right) I^{M}_{200}$$

$$\overbrace{\frac{dI^{M}_{500_{1st}}}{dt}}^{\text{Change in infecteds (CD4>500) during 1st treatment}} = \overbrace{\eta^{U}_{500} I^{M}_{500}}^{\text{Commenced 1st line therapy (CD4>500, Undetectable Viral Load}} + \overbrace{\psi_C I^{A}_{500_{1st}}}^{\text{Spontaneous HCV clearance (acute, CD4>500)}} + \overbrace{\omega^{U}_{350\_500} I^{M}_{350\_500_{1st}}}^{\text{Viral supression during 1st line therapy (350<CD4<500)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{500}}^{\text{HIV-related death (CD4>500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi_{500}}^{\text{Viral rebound (CD4>500)}} \right) I^{M}_{500_{1st}}$$

$$\overbrace{\frac{dI^{M}_{350\_500_{1st}}}{dt}}^{\text{Change in infecteds (350<CD4<500) during 1st treatment}} = \overbrace{\eta^{U}_{350\_500} I^{M}_{350\_500}}^{\text{Commenced 1st line therapy (350<CD4<500, Undetectable Viral Load}} + \overbrace{\psi_C I^{A}_{350\_500_{1st}}}^{\text{Spontaneous HCV clearance (acute, 350<CD4<500)}} + \overbrace{\omega^{U}_{200\_350} I^{M}_{200\_350_{1st}}}^{\text{Viral supression during 1st line therapy (200<CD4<350)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{350\_500}}^{\text{HIV-related death (350<CD4<500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi_{350\_500}}^{\text{Viral rebound (350<CD4<500)}} + \overbrace{\omega^{U}_{350\_500}}^{\text{Viral supression (350<CD4<500)}} \right) I^{M}_{350\_500_{1st}}$$

$$\overbrace{\frac{dI^{M}_{200\_350_{1st}}}{dt}}^{\text{Change in infecteds (200<CD4<350) during 1st treatment}} = \overbrace{\eta^{U}_{200\_350} I^{M}_{200\_350}}^{\text{Commenced 1st line therapy (200<CD4<350, Undetectable Viral Load}} + \overbrace{\psi_{C} I^{A}_{200\_350_{1st}}}^{\text{Spontaneous HCV clearance (acute, 200<CD4<350)}} + \overbrace{\omega^{U}_{200} I^{M}_{200_{1st}}}^{\text{Viral supression during 1st line therapy (CD4<200)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200\_350}}^{\text{HIV-related death (200<CD4<350)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi_{200\_350}}^{\text{Viral rebound (200<CD4<350)}} + \overbrace{\omega^{U}_{200\_350}}^{\text{Viral supression (200<CD4<350)}} \right) I^{M}_{200\_350_{1st}}$$

$$\overbrace{\frac{dI^{M}_{200_{1st}}}{dt}}^{\text{Change in infecteds (CD4<200) during 1st treatment}} = \overbrace{\eta^{U}_{200} I^{M}_{200}}^{\text{Commenced 1st line therapy (CD4<200, Undetectable Viral Load)}} + \overbrace{\psi_{C} I^{A}_{200_{1st}}}^{\text{Spontaneous HCV clearance (acute, CD4<200)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200}}^{\text{HIV-related death (CD4<200)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi_{200}}^{\text{Viral rebound (CD4<200)}} + \overbrace{\omega^{U}_{200}}^{\text{Viral supression (CD4<200)}} \right) I^{M}_{200_{1st}}$$

$$\overbrace{\frac{dI^{M}_{500_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (CD4>500)}} = \overbrace{\eta^{D}_{500} I^{M}_{500}}^{\text{Commenced 1st line therapy (CD4>500, Detectable Viral Load)}} + \overbrace{\psi_{C} I^{A}_{500_{Fail}}}^{\text{Spontaneous HCV clearance (acute, CD4>500)}} + \overbrace{\phi_{500} I^{M}_{500_{1st}}}^{\text{Viral rebound during 1st line therapy (CD4>500)}} + \overbrace{\phi^{S}_{500} I^{M}_{500_{2nd}}}^{\text{Viral rebound during 2nd line therapy (CD4>500)}} - \left(\overbrace{\mu}^{\text{Backgrou death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{500}}^{\text{HIV-related death (CD4>500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\omega^{D}_{500}}^{\text{Progress to (350<CD4<500)}} + \overbrace{\sigma_{500}}^{\text{Commence 2nd line therapy (CD4>500)}} \right) I^{M}_{500}$$

$$\overbrace{\frac{dI^{M}_{350\_500_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (350<CD4<500)}} = \overbrace{\eta^{D}_{350\_500} I^{M}_{350\_500}}^{\text{Commenced 1st line therapy (350<CD4<500, Detectable Viral Load)}} + \overbrace{\psi_{C} I^{A}_{350\_500_{Fail}}}^{\text{Spontaneous HCV clearance (acute, 350<CD4<500)}} + \overbrace{\phi_{350\_500} I^{M}_{350\_500_{1st}}}^{\text{Viral rebound during 1st line therapy (350<CD4<500)}} + \overbrace{\phi^{S}_{350\_500} I^{M}_{350\_500_{2nd}}}^{\text{Viral rebound during 2nd line therapy (350<CD4<500)}}$$

$$+ \overbrace{\omega^{D}_{500} I^{M}_{500_{Fail}}}^{\text{Progress from CD4>500 after 1st line treatment failure}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{350\_500}}^{\text{HIV-related death (350<CD4<500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} \right.$$

$$\left. + \overbrace{\omega^{D}_{350\_500}}^{\text{Progress to (200<CD4<350)}} + \overbrace{\sigma_{350\_500}}^{\text{Commence 2nd line therapy (350<CD4<500)}} \right) I^{M}_{350\_500_{Fail}}$$

$$\overbrace{\frac{dI^{M}_{200\_350_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (200<CD4<350)}} = \overbrace{\eta^{D}_{200\_350} I^{M}_{200\_350}}^{\text{Commenced 1st line therapy (200<CD4<350, Detectable Viral Load)}} + \overbrace{\psi_{C} I^{A}_{200\_350_{Fail}}}^{\text{Spontaneous HCV clearance (acute, 200<CD4<350)}} + \overbrace{\phi_{200\_350} I^{M}_{200\_350_{1st}}}^{\text{Viral rebound during 1st line therapy (200<CD4<350)}} + \overbrace{\phi^{S}_{200\_350} I^{M}_{200\_350_{2nd}}}^{\text{Viral rebound during 2nd line therapy (200<CD4<350)}}$$

$$+ \overbrace{\omega^{D}_{350\_500} I^{M}_{350\_500_{Fail}}}^{\text{Progress from 350<CD4<500 after treatment failure}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200\_350}}^{\text{HIV-related death (200<CD4<350)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} \right.$$

$$\left. + \overbrace{\omega^{D}_{200\_350}}^{\text{Progress to CD4<200}} + \overbrace{\sigma_{200\_350}}^{\text{Commence 2nd line therapy (200<CD4<350)}} \right) I^{M}_{200\_350_{Fail}}$$

$$\overbrace{\frac{dI^{M}_{200_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (CD4<200)}} = \overbrace{\eta^{D}_{200} I^{M}_{200}}^{\text{Commenced 1st line therapy (CD4<200, Detectable Viral Load)}} + \overbrace{\psi_{C} I^{A}_{200_{Fail}}}^{\text{Spontaneous HCV clearance (acute, CD4<200)}} + \overbrace{\phi_{200} I^{M}_{200_{1st}}}^{\text{Viral rebound during 1st line therapy (CD4<200)}}$$

$$+ \overbrace{\phi^{S}_{200} I^{M}_{200_{2nd}}}^{\text{Viral rebound during 2nd line therapy (CD4<200)}} + \overbrace{\omega^{D}_{200\_350} I^{M}_{200\_350_{Fail}}}^{\text{Progress from 200<CD4<350 after treatment failure}} - \left(\overbrace{\mu}^{\text{Background death}} \right.$$

$$\left. + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200}}^{\text{HIV-related death (CD4<200)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\sigma_{200}}^{\text{Commence 2nd line therapy (CD4<200)}} \right) I^{M}_{200_{Fail}}$$

$$\overbrace{\frac{dI^{M}_{500_{2nd}}}{dt}}^{\text{Change in infecteds (CD4>500) on 2nd line treatment}} = \overbrace{\sigma_{500} I^{M}_{500_{Fail}}}^{\text{Commence 2nd line therapy (CD4>500)}} + \overbrace{\psi_{C} I^{A}_{500_{2nd}}}^{\text{Spontaneous HCV clearance (acute, CD4>500)}} + \overbrace{\omega^{U}_{350\_500} I^{M}_{350\_500_{2nd}}}^{\text{Viral supression during 2nd line therapy from 350<CD4<500}}$$

$$- \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{500}}^{\text{HIV-related death (CD4>500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi^{S}_{500}}^{\text{Viral rebound during 2nd line therapy (CD4>500)}} \right) I^{M}_{500_{2nd}}$$

$$\overbrace{\frac{dI^{M}_{350\_500_{2nd}}}{dt}}^{\text{Change in infecteds (350<CD4<500) on 2nd line treatment}} = \overbrace{\sigma_{350\_500} I^{M}_{350\_500_{Fail}}}^{\text{Commence 2nd line therapy (350<CD4<500)}} + \overbrace{\psi_{C} I^{A}_{350\_500_{2nd}}}^{\text{Spontaneous HCV clearance (acute, 350<CD4<500)}} + \overbrace{\omega^{U}_{200\_350} I^{M}_{200\_350_{2nd}}}^{\text{Viral supression during 2nd line therapy from 200<CD4<350}} - \left(\overbrace{\mu}^{\text{Background death}} \right.$$

$$\left. + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{350\_500}}^{\text{HIV-related death (350<CD4<500)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi^{S}_{350\_500}}^{\text{Viral rebound during 2nd line therapy (350<CD4<500)}} + \overbrace{\omega^{U}_{350\_500}}^{\text{Viral supression}} \right) I^{M}_{350\_500_{2nd}}$$

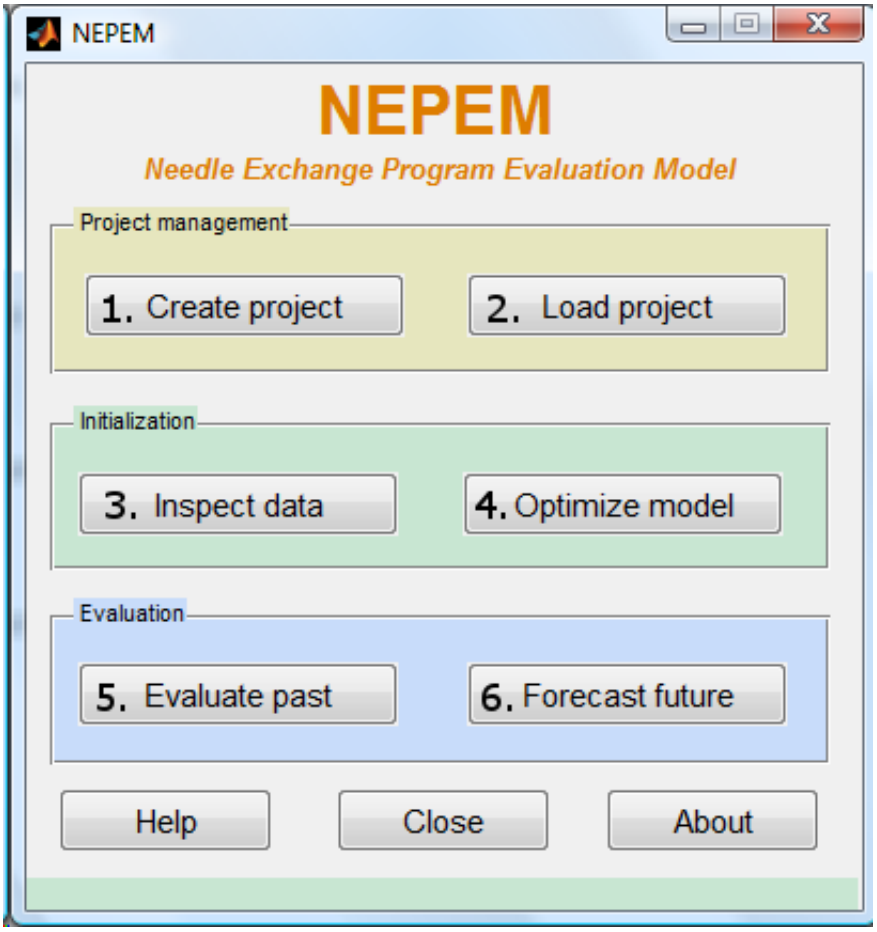
$$\overbrace{\frac{dI^{M}_{200\_350_{2nd}}}{dt}}^{\text{Change in infecteds (200<CD4<350) on 2nd line treatment}} = \overbrace{\sigma_{200\_350} I^{M}_{200\_350_{Fail}}}^{\text{Commence 2nd line therapy (200<CD4<350)}} + \overbrace{\psi_{C} I^{A}_{200\_350_{2nd}}}^{\text{Spontaneous HCV clearance (acute, 200<CD4<350)}} + \overbrace{\omega^{U}_{200} I^{M}_{200_{2nd}}}^{\text{Viral supression during 2nd line therapy from CD4<200}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200\_350}}^{\text{HIV-related death (200<CD4<350)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi^{S}_{200\_350}}^{\text{Viral rebound during 2nd line therapy (200<CD4<350)}} + \overbrace{\omega^{U}_{200\_350}}^{\text{Viral supression}} \right) I^{M}_{200\_350_{2nd}}$$

$$\overbrace{\frac{dI^{M}_{200_{2nd}}}{dt}}^{\text{Change in infecteds (CD4<200) on 2nd treatment}} = \overbrace{\sigma_{200} I^{M}_{200_{Fail}}}^{\text{Commence 2nd line therapy (CD4<200)}} + \overbrace{\psi_{C} I^{A}_{200_{2nd}}}^{\text{Spontaneous viral clearance (acute, CD4<200)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{D}}^{\text{Drug-related death}} + \overbrace{\xi}^{\text{Exit rate}} + \overbrace{\mu_{200}}^{\text{HIV-related death (CD4<200)}} + \overbrace{\lambda_{HCV}}^{\text{Force of HCV infection}} + \overbrace{\phi^{S}_{200}}^{\text{Viral rebound during 2nd line therapy (CD4<200)}} + \overbrace{\omega^{U}_{200}}^{\text{Viral supression}} \right) I^{M}_{200_{2nd}}$$

Needle Exchange Program Evaluation Model (NEPEM) Software

The NEPEM software was produced as a front-end to the model; this software can be downloaded from http://www.natcent.unsw.edu.au/sepph/software.html. The series of steps for using the software are shown in the following section. The software can be invoked by running BasePage.m from the Matlab interpreter.

Main menu

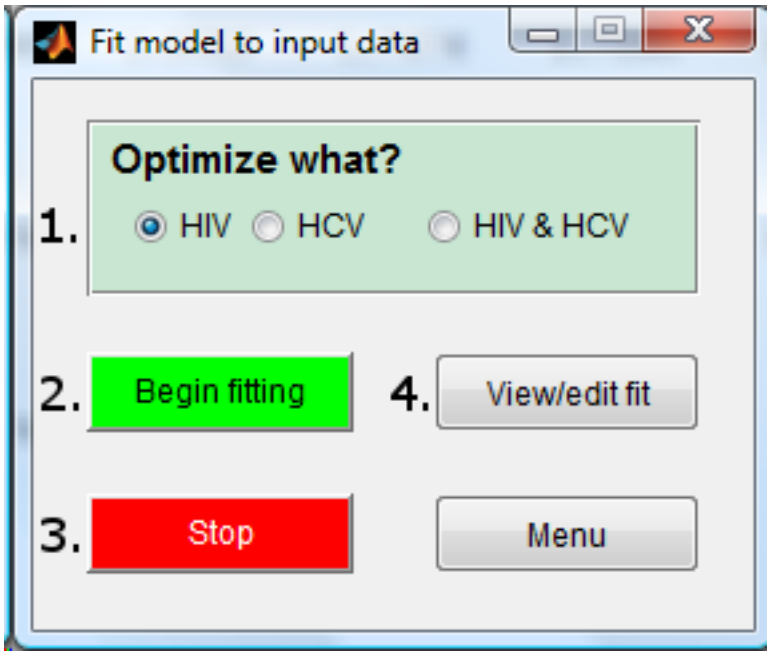


1. The Create new project button, this will open a dialogue box for the user to enter the name for the project. Next the user will be prompted to select an input file to populate the project.
2. The Load project button, by default all projects are saved in the 'Projects' folder in the root directory of the program. Select the .mat corresponding to the project you wish to run. Note, within the Projects folder, sub folders with the name

<Project name>_DataFiles will be present, users do not need to select these folders.

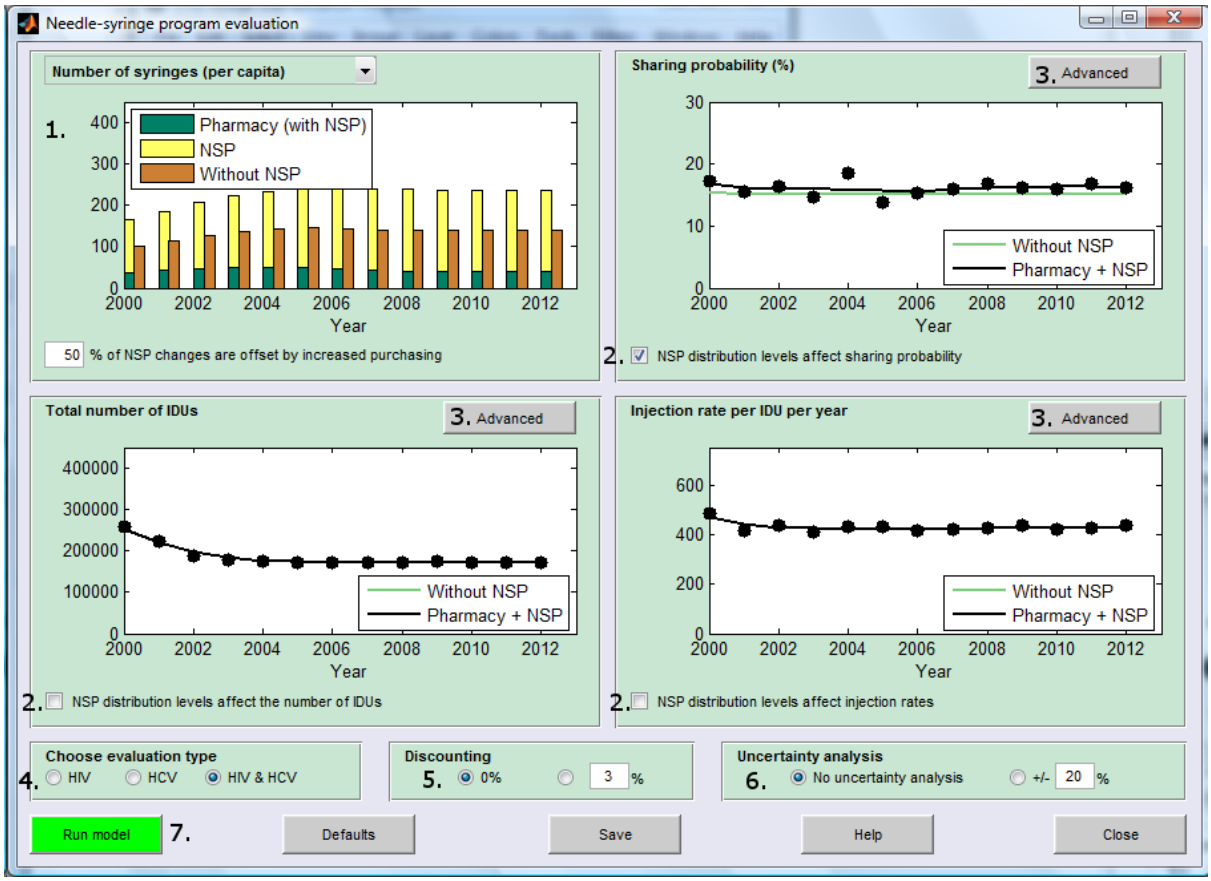
3. This button allows users to view a series of plots of the data contained in the project file, here they may double check the data.
4. This button will launch the Optimize model screen. See the Optimize Model section for more details.
5. This button launches the Economic analysis screen. See the Economic Analysis section for more details.
6. This button launches the Forecasting screen. See the Forecast section for more details.

Optimize Model

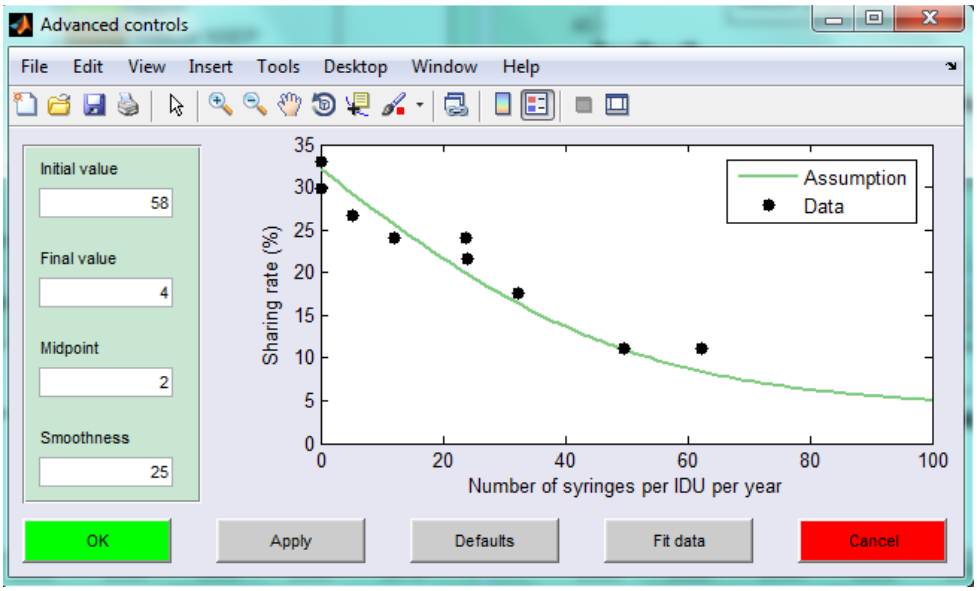


1. Select optimization for HIV, HCV, or both.
2. The Begin fit button will start the fitting process
3. The Stop button will halt the fitting process. Note, that it will not immediately stop the program, and must complete the set it is working on to ensure quality of results. Further, if you have selected 'Both' the stop button will only effect the current fit, so users may have to push it a second time to halt HCV fitting.
4. This will open a manual fitting page, where users can enter parameter values and observe the effect on the fit. Recommended for advanced users only.

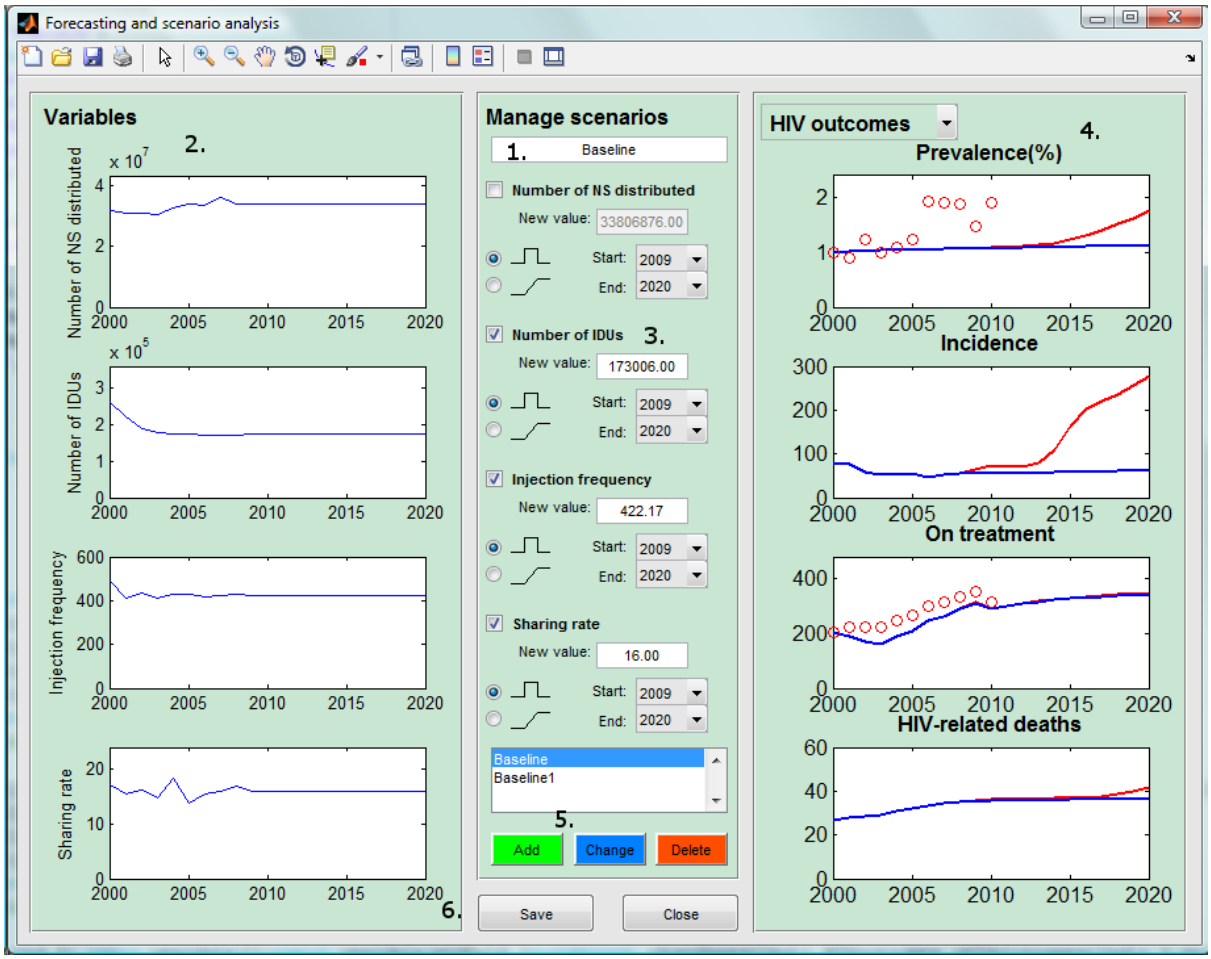
Economic Analysis



1. Panels which contain the parameters that can be used to evaluate the effectiveness of Needle-syringe programs.
2. Checkboxes select whether the parameter will be effected by the distribution of NSPs.
3. Advanced options for determining the shape of the green line. **This is one of the most important features of the software, from which associations between sharing levels and per capita needle-syringe distributions are determined (see below). This forms a key assumption in the counterfactual scenario. The other key assumption is the percentage of NSP changes that are offset by increased purchasing (value entered in top left panel above).**
4. Select the evaluation type.
5. Select discounting option.
6. Choose whether or not to run a small sensitivity analysis.
7. Runs the model. Once complete, the user will be presented with plots of the fitting, and the option to view further plots, or a summary table of economic outcomes.


Advanced controls
File Edit View Insert Tools Desktop Window Help
Initial value
58
Final value
4
Midpoint
2
Smoothness
25
Assumption
Data
Sharing rate (%)
Number of syringes per IDU per year
0
5
10
15
20
25
30
35
0
20
40
60
80
100
OK
Apply
Defaults
Fit data
Cancel

Forecast



1. Enter the name of the scenario.
2. Plots of the variables used for the outcomes.
3. Properties of the variables that can be edited. Checkboxes determine whether the given variable will be applied. The 'New value' field determines the datapoint that the variable will use. The radio buttons determine the transition to the new value, sudden, or linear. The Start and End years determine the period of time that the 'New value' is applied for.
4. The plot of the outcomes. The drop down list allows users to switch between HCV and HIV outcomes.
5. When variable properties are set, users add the scenario to the list. This will plot the outcome on the right hand side. To edit a scenario, select it in the list and press the Change button. The Delete button removes the selected scenario.
6. The Save button will save an Excel file of the results shown in the outcome plots.

Data entry

A template spreadsheet is provided for users to input data for the model. This helps ensure correct formatting for the program to read in the data. In cases where some data are incomplete, the software will fill in gaps using interpolation. In cases where there is only one datum point, the software will assume it to be a constant for the entire time series. Although users can enter data for males and females, there are no separate categories for sex in the model. The software will use a weighted average based on the population figures to determine an 'overall' number to be used inside the model. All behavioral, epidemiological, clinical, economic and NSP data used in the model is specific to the setting in which the model is applied. All of these data are entered in the template spreadsheet.

Country data inputs

We identified data custodians or appropriate M&E representatives for each country and invited them (approximately 40 people) to a regional workshop (in Chisanau, Moldova). A three day training meeting was conducted to specifically discuss data issues - including representativeness, reliability, validity, comparisons within and across settings etc. Then there was an extensive period of data collation, with frequent periodic teleconferences between data collators in-country and external epidemiologists and reviewers to discuss these issues and the interpretation of available data. This was followed by another regional workshop, 9 months later (in Minsk, Belarus), with the purpose of comparing data sources between countries, and rigorously assessing the quality of data collection, their reliability and how they should be interpreted for use in the analyses. These exercises revealed that surveillance mechanisms differed between settings and even within countries there were inconsistencies in some data collection procedures, sampling frameworks etc. Based on this, we obtained disaggregated data from individual studies within countries and attempted to examine subsets of study data that are consistent across studies so that trends could be assessed as reliably as possible. In general, epidemic data was obtained from HIV surveillance systems from each individual country, whereas demographic and behavioural data was obtained through Integrated Biological and Behavioural Surveillance or similar surveys.

Cost data were sourced directly from the principal recipients and sub-recipients for each country. Estonia, Tajikistan (Central Asia AIDS Control Project (CAAP), Central Asian Regional HIV/AIDS Programme (CARHAP) and Open Society Institute - Assistance Foundation, Tajikistan) and Kazakhstan reported other sources (non-GFATM) of cost data. Data collected included all needle-syringe programs funded by countries' government, community and international donors. We collated all direct costs associated with NSPs including direct medical costs of staff, specialist, cost of needle and syringes, operational costs of NSP clinics and monitoring and evaluation costs for the programs. All data was integrated to a central database supervised by in-country collaborators. The data was thoroughly checked and its reliability was validated through a data triangulation process.

Table S2. Demographic and Intervention data collected from countries

Number of needles-syringes distributed						
	2005	**2006**	**2007**	**2008**	**2009**	**2010**
Armenia	69,264	59,690	73,630	78,235	78,268	140,000
Belarus	368,051	1,221,324	2,668,392	1,655,971	1,671,477	2,327,270
Estonia	865,452	1,616,235	2,005,951	2,420,304	2,277,509	2,925,545
Georgia	300,372	350,340	376,480	462,883	484,785	1,064,372

Kazakhstan	14,400,000	17,055,463	17,069,000	21,081,762	27,277,384	21,015,446
Moldova	1,951,160	2,207,536	1,897,906	1,871,976	1,687,972	1,600,000
Tajikistan	679,417	1,936,213	1,573,604	1,961,966	1,902,763	2,207,173
Ukraine	3,500,000	6,945,251	6,864,699	9,398,456	14,363,378	18,084,503
Russia-Kursk	40,297	39,834	104,360	326,440	490,720	686,560
Russia-Lipetsk	81,637	194,431	151,580	199,170	291,068	286,020
Population of PWID*						
Armenia	9,000	9,450	9,950	10,500	11,000	12,700
Belarus	45,842	51,000	52,062	53,124	55,247	56,043
Estonia	15,000	15,000	15,000	15,000	15,000	15,000
Georgia	40,000	40,000	40,000	40,000	40,000	40,000
Kazakhstan	128,200	128,200	128,800	129,100	124,400	122,700
Moldova	25,000	25,000	25,000	25,000	25,000	25,000
Tajikistan	25,000	25,000	25,000	25,000	25,000	25,000
Ukraine	290,000	290,000	290,000	290,000	290,000	290,000
Russia-Kursk	4,026	4,430	4,872	5,359	5,895	6,484
Russia-Lipetsk	5,275	5,839	6,457	6,563	7,451	8,345
Percentage of PWID accessing NSPs						
Armenia	5.00%	6.00%	7.00%	8.00%	9.00%	10.00%
Belarus	11.20%	15.20%	20.30%	24.80%	26.60%	30.60%
Estonia	73.00%	75.00%	77.00%	78.50%	80.00%	80.00%
Georgia	2.00%	5.00%	8.00%	10.00%	10.00%	10.00%
Kazakhstan	23.00%	29.00%	29.00%	35.00%	47.00%	62.00%
Moldova	21.40%	23.70%	25.50%	26.80%	39.70%	42.20%
Tajikistan	11.60%	18.20%	17.60%	19.20%	27.20%	33.40%
Ukraine	12.00%	19.30%	23.30%	32.60%	52.00%	58.60%
Russia-Kursk	15.60%	9.30%	12.20%	35.50%	50.20%	54.90%
Russia-Lipetsk	--	--	--	--	--	--

* Demographic data were mostly taken from population size estimates that had been done in the region in 2009. Population sizes of PWID are always extremely difficult. There is no way to know how accurate they are in any setting. These estimates are crucial for determining the extent of the epidemic overall, coverage of interventions, and overall impact of their implementation – both epidemiologically and economically. Each country had official population size estimates. These official estimates, produced by different processes, generally had acceptable rationale behind them and were used for our analyses unless there were good reasons to believe that they were not reliable.

Table S3. Epidemiological data associated with PWID collected from countries. All prevalence levels and HIV testing coverage rates have uncertainties bounds provided by in-country collaborators. An implicit ±25% uncertainty level was assumed in the model when uncertainty was not provided.

Armenia

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
HIV											
HIV prevalence						8.77% (7.92-9.62%)		6.41% (5.85-6.98%)			9.70% (4.80-15.80%)
HIV diagnoses	18	19	22	12	33	46	24	32	35	44	38
AIDS diagnoses	3	4	1	12	20	41	46	59	83	84	94
On first-line ART	0	0	0	0	0	15	28	31	38	60	90
Tested in last 12 months						20.18%		23.58%			18.10%
Treatment-eligible			206	232	254	161	167	125	126	122	182
On second-line ART	0	0	0	0	0	0	0	2	4	5	7
HCV											
HCV prevalence											36.4% (26.9-45.5%)
Receive HCV treatment	0	0	0	0	0	0	0	0	0	0	0
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Belarus

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
HIV											
HIV prevalence					9.7% (9.1-10.3%)		15.4% (14.6-16.2%)		7.7% (6.9-8.5%)	10.3% (9.5-11.1%)	
HIV diagnoses	378	414	584	448	360	276	242	298	195	212	223
AIDS diagnoses						79	205	192	221	245	274
On first-line ART	0	0	0	0	0	77	310	396	517	655	612
Tested in last 12 months						45.9%	51.6%	59.2%		65.8%	
Treatment-											

eligible											
On second-line ART	0	0	0	0	0	0	0	0	0	0	0
HCV											
HCV prevalence							39.0% (38.2-39.8%)				
Receive HCV treatment	0	0	0	0	0	0	0	0	0	0	0
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Estonia

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence				45% (38-51%)	55% (45-66%)	54% (47-60%)		54% (47-61%)		48% (42-53%)	
HIV diagnoses	354	1339	702	833	722	618	654	622	417	308	175
AIDS diagnoses	0	0	2	6	18	17	23	45	41	25	
On first-line ART											1,100
Tested in last 12 months						52%		43%		36%	
Treatment-eligible											
On second-line ART											
HCV											
HCV prevalence						80% (74-84%)		95% (92-97%)		95%	
Receive HCV treatment	0	0	0	0	0	0	0	0	0	0	0
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Georgia

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence	1.1%		1.1%		1.5% (0.4-		1.8% (0-			2.1% (0-	

*					2.1%)		3.6%)			4.5%	
HIV diagnoses	79	93	95	100	163	242	276	344	351	385	455
AIDS diagnoses	49	40	43	64	105	147	158	201	203	193	148
On first-line ART	96	106	118	131	146	162	180	200	222	294	363
Tested in last 12 months	5%		5%		5%		5%			5%	
Treatment-eligible											
On second-line ART	17	19	21	24	26	29	32	36	40	43	65
HCV											
HCV prevalence	70%		70%				64.6%	56.8%	50%	50%	50%
Receive HCV treatment	250	255	260	265	270	275	280	285	290	320	320
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

* It is believed that these prevalence estimates under-estimate the true prevalence level among PWID in Georgia

Kazakhstan

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence				3.9% (2.7-5.1%)	2.8% (2.2-3.4%)	2.9% (2.4-3.4%)	3.4% (2.9-3.9%)	3.9% (3.4-4.4%)	4.2% (3.6-4.8%)	2.9% (2.4-3.4%)	2.8% (2.3-3.3%)
HIV diagnoses	295	1032	515	501	433	632	1159	1258	1410	1150	1043
AIDS diagnoses											
On first-line ART							195 (174-216)	246 (222-270)	307 (284-330)	498 (470-526)	639 (623-655)
Tested in last 12 months							56%	49%	57%	61%	65%
Treatment-eligible							386 (347-425)	562 (516-608)	538 (495-581)	863 (811-915)	713 (664-762)
On second-line ART							10 (4-16)	13 (6-20)	16 (8-24)	26 (16-36)	34 (23-45)
HCV											
HCV prevalence				56.7% (53.7-59.7%)	57.8% (56.0-59.6%)	63.1% (61.7-64.5%)	64.5% (63.1-65.9%)	65.7% (64.4-67.7%)	64.1% (62.8-65.5%)	60.3% (58.9-61.7%)	59.0% (57.6-60.4%)
Receive	0	0	0	0	0	0	0	0	0	0	0

HCV treatment											
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Moldova

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence		29%			25.3% (21.0-29.6%)			20.0% (15.4-24.6%)		17.8%	
HIV diagnoses	174	232	199	253	357	533	618	731	790	704	704
AIDS diagnoses	5	7	18	43	53	62	85	189	82	277	92
On first-line ART				17	72	107	154	229	299	367	389
Tested in last 12 months		40%			42-52%			33-58%		41-49%	
Treatment-eligible	744	921	1085	1232	1172	963	979	1750	1583	1577	
On second-line ART								3	4	13	
HCV											
HCV prevalence								43.4% (37.7-49.1%)		63%	
Receive HCV treatment	0	0	0	0	0	0	0	0	0	0	0
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Tajikistan

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence						16.6% (13.3-20.4%)	22.6% (18.9-26.7%)	19.8% (17.6-22.1%)	17.6% (15.5-19.9%)	17.7% (15.8-19.7%)	
HIV diagnoses	6	19	22	36	144	130	97	152	180	220	595
AIDS diagnoses	0	0	0	0	1	0	0	6	21	53	44
On first-line ART	0	0	0	0	0	0	41	30	102	167	272
Tested in last 12	0%	0%	0%			21.3-37.6%	22.6-29.2%	28.7-36.2%	29.3-39.7%	27.7-42.2%	

months											
Treatment-eligible											
On second-line ART											
HCV											
HCV prevalence						46.9% (42.2-51.6%	44.3% (39.8-49.0%)	30.8% (28.3-33.5%)	30.4% (27.8-33.1%)	32.9% (30.5-35.4%)	
Receive HCV treatment	0	0	0	0	0	0	0	0	0	0	22
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Ukraine

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence	32.0% (29.3-34.7%)				29.1% (26.7-31.5%)	30.0% (28.2-31.8%)	42.9% (40.8-45.0%)	30.6% (28.7-32.5%)	29.1% (27.4-30.8%)	20.5% (19.1-21.9%)	20.5% (19.1-21.9%)
HIV diagnoses	3881	3984	4587	4815	5778	6270	7127	7084	7009	7015	
AIDS diagnoses	405	491	711	927	1271	1920	2095	1835	1623	1592	
On first-line ART	0	0	0	0	0	0	0	0	0	1194	1732
Tested in last 12 months					30%		23%	31,2%	30.5%	27.6%	27.6%
Treatment-eligible										902	834
On second-line ART	0	0	0	0	0	0	0	0	0	0	0
HCV											
HCV prevalence							50.7%				
Receive HCV treatment	0	0	0	0	0	0	0	0	252	256	
Receive liver transplant	0	0	0	0	0	0	0	0	0	0	0

Russia-Kursk

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											

HIV prevalence	0.8%	1.1%	1.5%	1.5%	1.6%	1.8%	2.0%	2.0%	2.0%	2.0%	2.1%
HIV diagnoses	10	10	13	7	10	12	11	11	13	11	17
AIDS diagnoses	0	0	0	2	4	5	7	4	4	7	11
On first-line ART					1	1	1	2	8	1	4
Tested in last 12 months	9.4%	23.1%	10.5%	13.2%	18.8%	36.5%	33.2%	18.9%	18.5%	20.8%	15.6%
Treatment-eligible			1		2	1	5	4	12	8	15
On second-line ART					1	1	1	2	8	1	4
HCV prevalence							53.0%	50.0%	47.0%	48.0%	57.5%
Receive HCV treatment										5	23
Receive liver transplant											

Russia-Lipetsk

	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2010**
HIV											
HIV prevalence						2.0%	3.5%	3.5%	3.5%	3.5%	3.5%
HIV diagnoses	9	13	4	6	7	8	28	20	11	8	
AIDS diagnoses											
On first-line ART											
Tested in last 12 months											
Treatment-eligible											
On second-line ART											
HCV prevalence						77.4%	80.1%	80.4%	78.3%	84.0%	78.2%
Receive HCV treatment											
Receive											

liver transplant											

Table S4. Behavioral data associated with PWID collected from countries. All behavioural indicators have uncertainties bounds provided by in-country collaborators. An implicit ±25% uncertainty level was assumed for these indicators in the model when uncertainty was not provided.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Armenia											
Average frequency of monthly injecting*			18			15		12			12
% shared syringe last month			44% (33-55%)			31.1% (23.3-38.9%)		33.3% (25.0-41.6%)			36.1% (27.1-45.1%)
% injections shared for sharing PWID											
% shared syringes cleaned						43.6% (32.7-54.5%)		37.8% (28.4-47.3%)			63.8% (47.9-79.8%)
Belarus											
Average frequency of monthly injecting*							14			13	
% shared syringe last month						19.6%	10.8%	7.6%		6%	
% injections shared for sharing PWID											
% shared syringes cleaned											
Estonia											
Average frequency of monthly injecting*						39		49		39	
% shared syringe last month						27% (22-33%)		24% (20-30%		24% (19-30%)	

% injections shared for sharing PWID						1.5% (1.4-1.7%)		1.3% (1.2-1.5%)		2% (1.7-2.2%)	
% shared syringes cleaned											
Georgia											
Average frequency of monthly injecting*											
% shared syringe last month	38.1%		38.1%		39.1%		30.0%		25.0%	25.0%	15.0%
% injections shared for sharing PWID											
% shared syringes cleaned	10.0%		10.0%		10.0%		10.0%				
Kazakhstan											
Average frequency of monthly injecting*						40 (38-42)	41 (39-43)	36 (34-38)	35 (33-37)	30 (28-32)	29 (27-30)
% shared syringe last month					14.4% (19.5-25.0%)	17.1 (18.2-19.4%)	15.6% (14.5-16.6%)	14.0% (13.0-15.1%)	16.7% (15.6-17.9%)	11.7% (10.8-12.8%)	9.3% (8.5-10.3%)
% injections shared for sharing PWID						43.7% (40.4-47.0%)	45.5% (41.8-49.2%)	35.6% (31.8-39.3%)	31.7% (28.3-35.2%)	32.2% (28.1-36.4%)	43.2% (38.2-48.1%)
% shared syringes cleaned						83.1% (82.5-83.7%)	75.0% (74.3-75.7%)	71.0% (70.1-71.9%)	65.0% (64.0-68.0%)	78.8% (77.8-79.8%)	74.7% (73.6-75.8%)
Moldova											
Average frequency of monthly injecting*		24 (19-29)			38 (30-45)			15 (12-18)		12 (10-14)	
% shared syringe last month											

% injections shared for sharing PWID					15.3% (12.3-18.4%)			3.6% (2.9-4.3%)		1.5% (1.2-1.8%)	
% shared syringes cleaned		2.2% (1.8-2.6%)			13.3% (10.6-16.0%)						
Tajikistan											
Average frequency of monthly injecting*						21	29	24	19	22	
% shared syringe last month						37.7% (33.2-42.4%)	13.2% (10.4-16.7%)	17.7% (15.7-20.0%)	18.9% (16.8-21.3%)	19.1% (17.2-21.3%)	
% injections shared for sharing PWID											
% shared syringes cleaned						22.6% (18.9-26.9%)	24.3% (21.5-33.6%)	12.5% (10.8-14.6%)	8.1% (6.7-9.9%)	17.4% (15.5-19.4%)	
Ukraine											
Average frequency of monthly injecting*							24	26	25	21	21
% shared syringe last month			34.4%		26.9%		16.0%	22.7%	15.1%	9.9%	9.9%
% injections shared for sharing PWID											
% shared syringes cleaned											
Russia-Kursk											
Average frequency of monthly injecting*		15		11	13	21	18	36	43	66	52
% shared syringe		72.0%		62.3%	48.4%	39.3%	8.4%	11.5%	6.1%	3.2%	8.0%

last month											
% injections shared for sharing PWID		85.7%		85.7%	87.1%	89.3%	78.3%	92.3%	89.8%	90.3%	78.0%
% shared syringes cleaned		36.8%		35.7%	32.3%	21.4%	1.2%	9.6%	5.1%	3.2%	8.0%
Russia-Lipetsk											
Average frequency of monthly injecting*							39	50	55	62	77
% shared syringe last month							30%	35%	13%	2%	8%
% injections shared for sharing PWID											
% shared syringes cleaned											
*: Weighted average over distribution of categories of injecting frequencies; distributions and confidence limits not shown here											

Investments in NSPs

There were limited costing data on HIV prevention and treatment programs among PWID. Previous cost studies and program reports suggest that the average unit costs of providing NSP services to PWID range from $0.11 in China [4] to $0.36 in Belarus [5] and $0.43 in Ukraine [6]. Studies on the costs of ART in countries of EECA present varying costs across the different countries. A World Bank study in 2007 reported annual costs of $200 to $3,600 per person, with an unweighted average of $1,600 per person, and other healthcare related costs amounting to an average of $570 per person [7].

The average cost of reaching one PWID through NSPs across all the eight countries rose from $47.4 in 2005 to $62.3 in 2010; Belarus and Moldova were the only countries to have decreasing trends over time.

Table S5. Total investments in NSP per country (in US$)

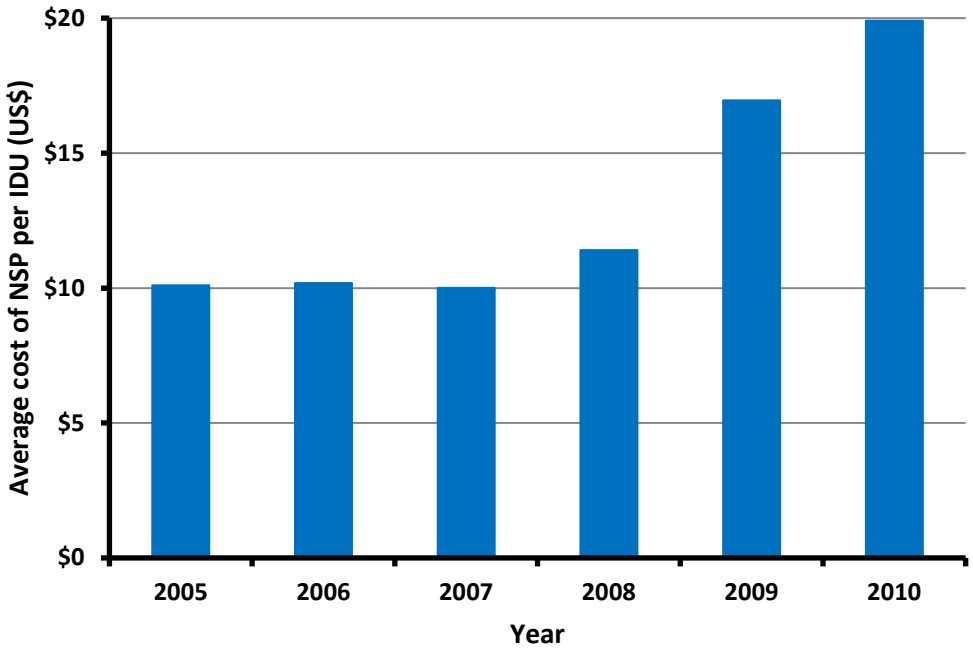
	2005	2006	2007	2008	2009	2010
Armenia	30,303	30,303	30,303	30,303	42,152	54,000
Belarus	225,878	584,847	618,126	605,502	623,412	814,950
Estonia	774,321	902,500	1,229,712	1,361,390	1,276,258	1,276,957
Georgia	60,241	106,515	114,887	193,391	270,000	446,000
Kazakhstan	1,669,241	2,301,766	2,406,926	2,589,761	3,172,652	4,128,319
Moldova	262,033	330,054	234,074	273,440	267,278	251,690
Tajikistan	74,736	269,483	359,449	588,803	608,462	931,223
Ukraine	152,523	1,673,978	1,296,453	1,480,685	4,148,721	4,290,378
Russia-Kursk	5,447	24,002	27,362	52,923	48,061	41,246
Russia-Lipetsk	22,640	43,348	52,083	59,469	55,832	61,209

Table S6. Cost per PWID covered per country per year (in US$)

	2005	2006	2007	2008	2009	2010
Armenia	3.4	3.2	3.0	2.9	3.8	4.8
Belarus	4.9	11.5	11.9	11.4	11.3	14.5

Estonia	43.6	45.6	55.7	64.4	61.3	61.2
Georgia	1.5	2.7	2.9	4.8	6.8	11.2
Kazakhstan	13.0	18.0	18.7	20.1	25.5	33.6
Moldova	10.5	13.2	9.4	10.9	10.7	10.1
Tajikistan	3.0	10.8	14.4	23.6	24.3	37.2
Ukraine		5.8	4.5	5.1	14.3	14.8
Russia-Kursk	1.4	5.4	5.6	9.9	8.2	6.4
Russia-Lipetsk	4.3	7.4	8.1	9.1	7.5	7.3

Figure S2. Average cost of NSPs per PWID across nine countries



Costs of ART

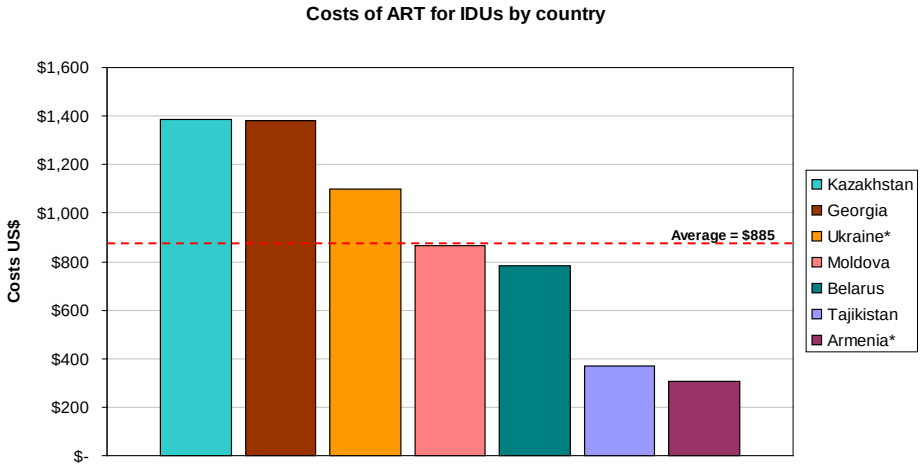
The dominant health costs for PWID living with HIV are associated with ART. There has been a steep decline in the price of first- and second-line regimens of ART in most (but not all) low- to middle-income countries between 2008 and 2010, by as much as 80% in some cases [8]. As most of the countries in this region are of these income classifications, we deduced that the costs of these drugs have also decreased. If applicable, other cost data on ART were derived from the ministries of health or the national AIDS centers in the countries. Interpolation and extrapolation were used for some missing data.

The cost of ART ranged from $308 in Armenia to $4,588 in Estonia. Excluding Estonia, the cost of ART in the other seven countries was relatively consistent, at an average of $885 per person per year. Estonia reported unit costs for ART of $4,588 per person year, but the GDP per capita ($14,403) is the highest among the countries analyzed. Estonia is not a recipient of the GFATM grants for harm reduction and has to purchase ARVs at the prevailing market price of the rest of Europe. Estonia also does not buy antiretroviral drugs in large quantities compared with counterpart countries in the region. The cost breakdown shows that the cost of first and second line ARV drugs contributed the most to the overall cost of ART in each country, followed by hospital costs and the cost of laboratory tests and viral load. The distribution of costs (excluding Estonia) is shown in Figure 1.

These regional costs are higher than those reported for low and middle-income countries. UNAIDS has published differential costs for low-income and middle-income countries. There are three major components for the costs of antiretroviral therapy; drugs, laboratory and service delivery. The cost of both 1st and 2nd line drugs for middle-income countries is reported in $155 for first line regimens and US$ 1,687 for second line regimens. Laboratory costs have been calculated as the annual median cost for laboratory tests across countries as obtained from recent literature. The median cost in 2010 is estimated at $180 (USD) per patient. Studies of service delivery costs found a range from $79 per patient per year to $345. The average cost (weighted across low income, lower middle, and upper middle-income countries) of about $180 per patient per year in 2010. Thus, the annual cost for antiretroviral treatment used in the UNAIDS investment framework amounts to (155+180+180) US$ 550 per person per year [9].

In some countries it is possible to determine the number of people who initiated ART after acquiring HIV infection through injecting drug use. However, most of the time assumptions need to be made on the proportion of all people initiating ART who are, or were, PWID. ART is often more likely withheld from PWID compared to other population groups due to fears of non-adherence and development of resistance; however, evidence has shown that the risk of development of antiretroviral resistance does not differ significantly between PWID and non-PWID, nor are there differences in rates of loss to follow-up and treatment failure [10]. Similarly, there is no evidence of increased sexual risk behavior after initiating ART among PWID [11].

Figure S3. ART costs per injecting drug user on treatment by country


Costs of ART for IDUs by country
$1,600
$1,400
$1,200
$1,000
$800
$600
$400
$200
$-
Costs US$
Average = $885
Kazakhstan
Georgia
Ukraine*
Moldova
Belarus
Tajikistan
Armenia*

Non-ART healthcare costs

Table S7: Average non-ART healthcare costs per person per year

Healthcare costs for HIV	**Armenia**	**Belarus**	**Estonia**	**Georgia**	**Kazkhstan**	**Moldova**	**Tajikistan**	**Ukraine**	**Russia-Kursk**	**Russia-Lipetsk**
PLHIV who have CD4 count >500 cells per µl	53	285	422		283	38	78	218	388	570
PLHIV who have CD4 count 350-500 cells per µl	53	285	422		186	43	118	218	651	818
PLHIV who have CD4 count 200-350 cells per µl	53	356	511		283	204	197	218	1,458	1,349
PLHIV who have CD4 count <200 cells per µl	53	487	687		283	213	197	218	2,923	1,478
Average annual other non-ART healthcare costs (for people on ART)	53	503	1108	1000	283	464	164	218	1,470	1,445
Healthcare costs for HCV				*			**	*		
Acute hepatitis C						17996				
Pre-cirrhosis stage of chronic hepatitis C (fibrosis stage 0 to 3) – 1st year	548					406				
Pre-cirrhosis stage of chronic hepatitis C (fibrosis stage 0 to 3) – successive years										
Compensated cirrhosis (fibrosis stage 4)	2740					811				
Acute hepatitis C treatment										
Treatment of chronic HCV patients with pegylated interferon and ribavirin (24 weeks)										
Treatment of chronic HCV patients with pegylated interferon and ribavirin (48 weeks)										
Hepatocellular carcinoma	724									
Liver transplant (1st year)										
Liver transplant (subsequent years)										
Decompensated cirrhosis (liver failure)	14860									

***** $23,560 and $21,076 spent on HCV-related healthcare costs per year in Georgia and Ukraine respectively across entire HCV-infected populations

** Average annual cost per person per year of $2380 in Tajikistan

Health state utilities

Table S8: Health state utilities

HIV	**Low estimates**	**Upper estimates**	**Reference**
Health Utility of uninfected PWID	0.93	0.96	[12]
Health Utility of PLHIV with CD4 > 500	0.84	0.95	[13, 14]
Health Utility of PLHIV with CD4 is 350-500	0.84	0.93	[13, 14]
Health Utility of PLHIV with CD4 is 200-350	0.72	0.93	[13, 14]
Health Utility of PLHIV with CD4 < 200	0.60	0.85	[13, 14]
Health Utility of PLHIV on ART	0.70	0.90	[14-17]
HCV	**Low estimates**	**Upper estimates**	**Reference**
Health Utility of PLHCV at acute stage	0.64	0.89	[18]
Health Utility of PLHCV at F0 to F3 stage	0.64	0.89	[19-21]
Health Utility of PLHCV at F4 stage	0.62	0.88	[19-21]
Health Utility of PLHCV at liver failure stage	0.52	0.87	[19-21]
Health Utility of PLHCV at HCC stage	0.54	0.80	[20, 21]
Health Utility of PLHCV at liver transplant	0.64	0.89	[20, 21]

Model biological parameters

Table S9: HIV-related parameters

Symbol	Description	Values	References
Population			
π	Average rate of people entering PWID population	Determined dynamically based on the exit rate (ζ) and mortality rates (*μ*) to ensure the total population size matches to the data in each country	
Transmission			
β_{HIV}	Transmission probability of HIV per injection with a contaminated syringe	0.6-0.8%	[22, 23]
Disease progression of undiagnosed individuals without treatment			
$1/\tau_{CD4>500}$	Average time for undiagnosed (without ART) HIV-infected individuals to progress from CD4 count >500 to CD4 count 350-500	4.09 (3.79-4.42) years	[24]
$1/\tau_{350<CD4<500}$	Average time for undiagnosed (without ART) HIV-infected individuals to progress from CD4 count 350-500 to CD4 count 200-350	1.96 (1.81-2.13) years	
$1/\tau_{200<CD4<350}$	Average time for undiagnosed (without ART) HIV-infected individuals to progress from CD4 count 200-350 to CD4 count <200	1.96 (1.81-2.13) years	
Disease progression of HIV-infected individuals on treatment (detectable viral load)			
$1/\omega^{D}_{CD4>500}$	Average time for HIV infected individuals on ART with detectable viral load to progress from CD4 count >500 to CD4 count 350-500	10.99 (1.32-12.00) years	[25]
$1/\omega^{D}_{350<CD4<500}$	Average time for HIV infected individuals on ART with detectable viral load to progress from CD4 count 350-500 to CD4 count 200-350	6.38 (0.48-8.00) years	
$1/\omega^{D}_{200<CD4<350}$	Average time for HIV infected individuals on ART with detectable viral load to progress from CD4 count 200-350 to CD4 count <200	8.88 (0.51-10.00) years	
Disease progression on treatment (undetectable viral load)			
$1/\omega^{U}_{CD4<200}$	Average time for HIV infected individuals on ART with undetectable viral load to progress from CD4 count <200 to CD4 count 200-350	2.80 (2.33-3.58) years	[26]
$1/\omega^{U}_{200<CD4<350}$	Average time for HIV infected individuals on ART with undetectable viral load to progress from CD4 count 200-350 to CD4 count 350-500	1.42 (0.90-3.42) years	
$1/\omega^{U}_{350<CD4<500}$	Average time for HIV infected individuals on ART with undetectable viral load to progress from CD4 count 350-500 to CD4 count >500	2.20 (1.07-7.28) years	
Commencement of treatment			
$\eta^{D/U}_{CD4>500}$	Proportion of individuals with CD4 count **>500** that commence treatment for HIV each year	0.05	Experimental variable
$\eta^{D/U}_{350<CD4<500}$	Proportion of individuals with CD4 count **350-500** that commence treatment for HIV each year	0.2	
$\eta^{D/U}_{200<CD4<350}$	Proportion of individuals with CD4 count **200-350** that commence treatment for HIV each year	0.75-0.85	
$\eta^{D/U}_{CD4<200}$	Proportion of individuals with **CD4** count **<200** that commence treatment for HIV each year	0.85-0.95	
Stopping treatment (detectable viral load)			
ϕ_S	Percentage of individuals on ART who cease therapy each year	1-5%	Expert opinion
Response to treatment (undetectable viral load)			
ϕ	Percentage of individuals on ART to experience viral rebound per year	3-6%	[27]
Response to treatment (detectable viral load)			
$1/\sigma_{200<CD4<350}$	Average time after treatment failure for individuals with CD4 count **> 200** to go on second line ART	6-18 months	Experimental variable
$1/\sigma_{CD4<200}$	Average time for individuals on ART with CD4 count **<200** to go on second-line ART	2-3 months	
Mortality Rates (Detectable Viral Load)			
$\mu^{D}_{CD4>500}$	HIV-related death rate for patients with CD4 count >500 cells per μL and detectable viral load	0.051% (0.035-0.068%)	[28]
$\mu^{D}_{350<CD4<500}$	HIV-related death rate for patients with CD4 count 350-500 cells per μL and detectable viral load	0.128% (0.092-0.164%)	[28]

$\mu^{D}_{200<CD4<350}$	HIV-related death rate per 100 person-years for patients with CD4 count 200-350 cells per μL and detectable viral load	1.0% (0.2-2.0)%	[25, 28]
$\mu^{D}_{CD4<200}$	HIV-related death rate per 100 person-years for patients with CD4 count <200 cells per μL and detectable viral load	4.08 (0.30-7.86)%	
Mortality Rates (Undetectable Viral Load)			
$\mu^{U}_{CD4<200}$	HIV-related death rate for patients with CD4 count <200 cells per μL and undetectable viral load	Same as $\mu^{D}_{CD4<200}$	Experimental variable
$\mu^{U}_{200<CD4<350}$	HIV-related death rate for patients with CD4 count 200-350 cells per μL and undetectable viral load	Same as $\mu^{D}_{200<CD4<350}$	
$\mu^{U}_{350<CD4<500}$	HIV-related death rate for patients with CD4 count 350-500 cells per μL and undetectable viral load	Same as $\mu^{D}_{350<CD4<500}$	
$\mu^{U}_{CD4>500}$	HIV-related death rate for patients with CD4 count >500 cells per μL and undetectable viral load	Same as $\mu^{D}_{CD4>500}$	
Average duration of drug use			
ζ	Average duration of drug-use among injecting drug users in Eastern Europe and Central Asian countries. Cessation rate is approximated by $1/\zeta$	10-20 years	[29, 30]

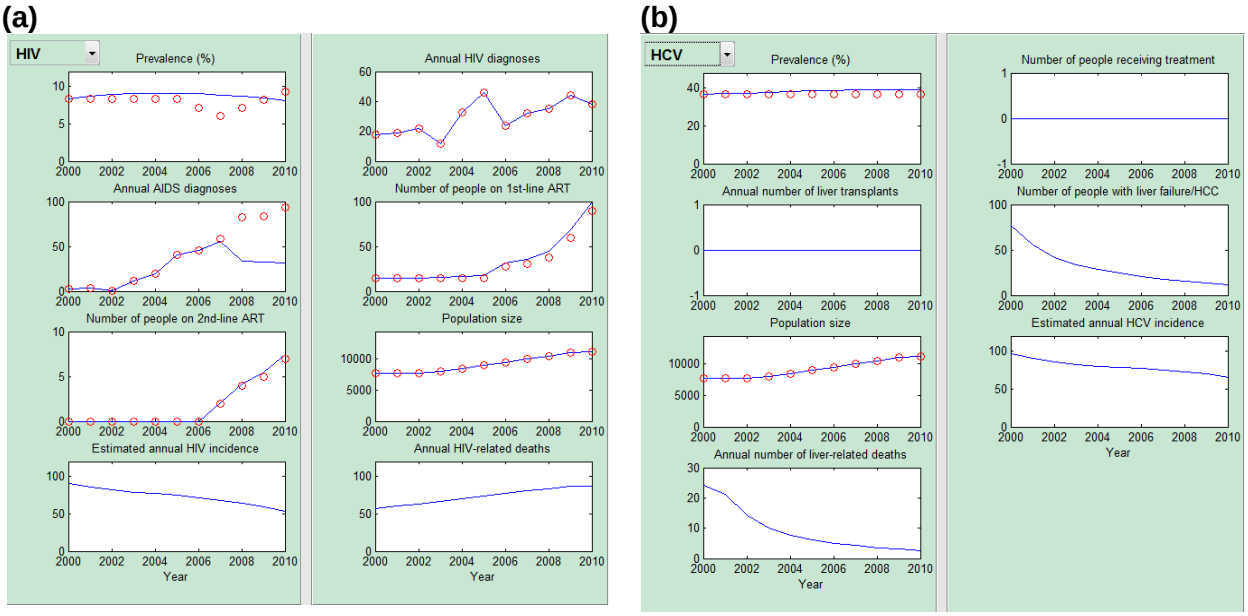
Table S10: HCV-related parameters

Symbol	Description		Values	References
Transmission				
β_{HCV}	Transmission probability of hepatitis C per injection with a contaminated syringe		1.5-4%	[31-38]
Disease progression without treatment				
$1/\tau_A$	Average time for untreated HCV infected individuals to progress from **acute** infection to the first stage of fibrosis (**F0)**		4-8 months	[39, 40]
$1/\tau_{F0-F1}$	Average time from fibrosis stage **F0** to **F1 [**Annual transition probability]		8.62 (0.23-16.95) years [0.116 (0.059-0.228)]	[41, 42]
$1/\tau_{F1-F2}$	Average time from fibrosis stage **F1** to **F2 [**Annual transition probability]		11.76 (9.09-15.38) years [0.085 (0.065-0.110)]	[41, 42]
$1/\tau_{F2-F3}$	Average time from fibrosis stage **F2** to **F3 [**Annual transition probability]		11.76 (6.80-20.41) years [0.085 (0.049-0.147)]	[41, 42]
$1/\tau_{F3-F4}$	Average time from fibrosis stage **F3** to **F4 [**Annual transition probability]		7.69 (3.13-18.87) years [0.130 (0.053-0.319)]	[41, 42]
$1/\tau_{F4-LF}$	Average time from **F4** to **liver failure [**Annual transition probability]		18.18 (10.87-25.0) years [0.055 (0.040-0.092)]	[43-59]
$1/\tau_{F4-HCC}$	Average time from **F4** to **hepatocellular carcinoma [**Annual transition probability]		32.26 (26.32-41.67) years [0.031 (0.024-0.038)]	
$1/\tau_{LF-HCC}$	Average time from **liver failure** to **hepatocellular carcinoma [**Annual transition probability]		14.71 (10.10-24.39) years [0.068 (0.041-0.099)]	[59, 60]
$1/\tau_{LF-LT}$	Average time from **liver failure** until **liver transplant [**Annual transition probability]		30.30 (20.41-58.82) years [0.033 (0.017-0.049)]	[61]
$1/\tau_{HCC-LT}$	Average time until **liver transplant** for individuals with **hepatocellular carcinoma [**Annual transition probability]		10.0 (5.56-20.0) years [0.1 (0.05-0.18)]	[62]
$1/\mu_{LF-LD}$	Average time until **liver-related death** for individuals with **liver failure [**Annual transition probability]		7.25 (4.95-13.51) years [0.138 (0.074–0.202)]	[48]
$1/\mu_{LT-LD}$	Average time until **liver-related death** for individuals who have received a **liver transplant [**Annual transition probability]	First year	5.92 (4.76-7.87) years [0.169 (0.127-0.210)]	[63, 64]
		After first year	29.41 (23.26-41.67) years [0.034 (0.024-0.043)]	
$1/\mu_{HCC-LD}$	Average time until **liver-related death** for individuals with **hepatocellular carcinoma [**Annual transition probability]		1.65 (1.48-1.83) years [0.605 (0.545-0.676)]	[52]
Commencement of treatment				
	Proportion treated for **Acute/Early** HCV infection		0.002-0.003	[62, 65]
$\frac{1}{\eta_A}$	Average time before individuals in **Acute/Early** HCV infection commence treatment	Asymptomatic	320 (213-399) days	Expert opinion
		Symptomatic	221 (188-274) days	
η_F	Proportion of individuals of fibrosis HCV infection to commence treatment per year	F0/1	25-30%	[66]
		F2/3	46-60%	
		F4	15-25%	
Stopping treatment				
$\frac{1}{\nu}$	Average duration of treatment	Acute	0.46 years	[67]
		F0-F4	0.69 years	[68, 69]
Clearance of virus				
ψ	Proportion of PWID who spontaneously clear HCV	Acute	0.26 (0.22-0.29)	[70]
γ_A	Proportion of HCV-treated individuals who clear the virus due to treatment (sustained virological responders) in **Acute** HCV		0.6-0.9	[71-75]
γ_{F0}	Proportion of HCV-treated individuals who clear the virus due to treatment in **F0** phase		0.60 (0.52-0.68)	[69, 76, 77]
γ_F	Proportion of HCV-treated individuals who clear the virus due to treatment in **F1-F4** phase		0.56 (0.50-0.61)	[69, 76, 77]

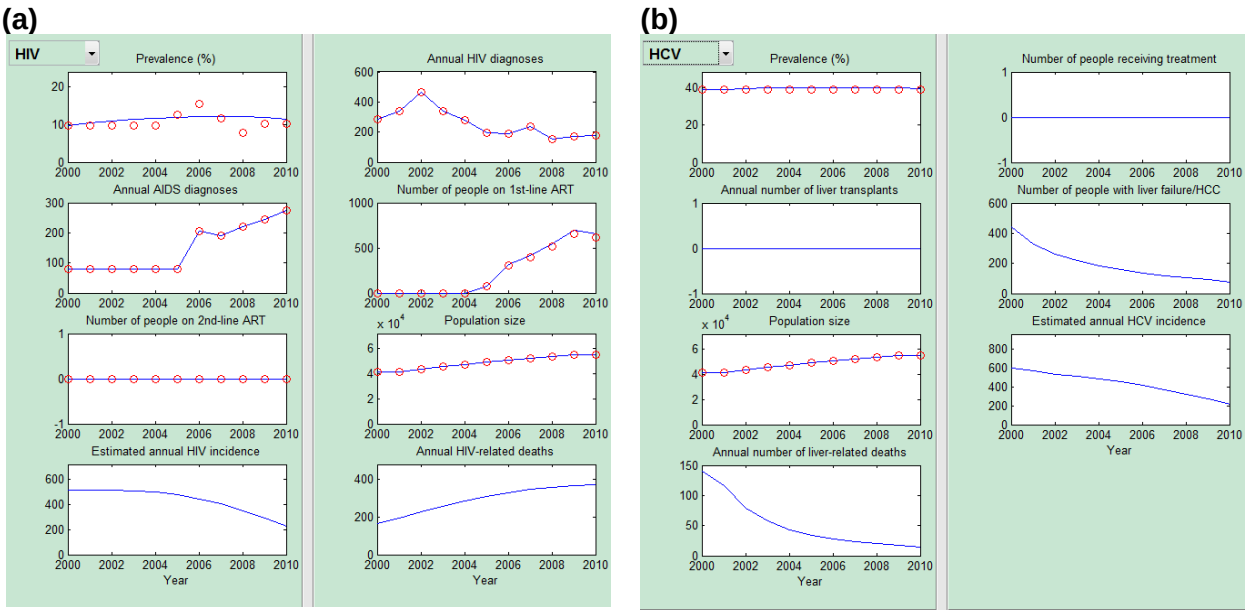
Calibration: model outcomes versus available data

Figure S4: Calibrated **(a)** HIV- and **(b)** HCV-related model trajectories (blue curves) compared with interpolated available data (red open circles) for each country.

Armenia

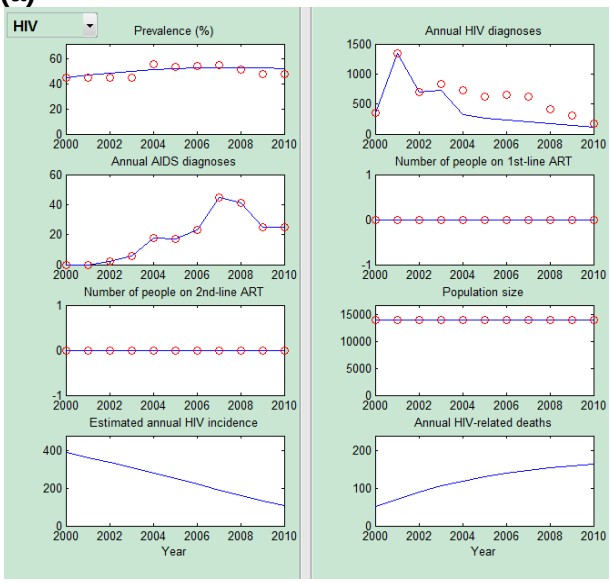


Belarus

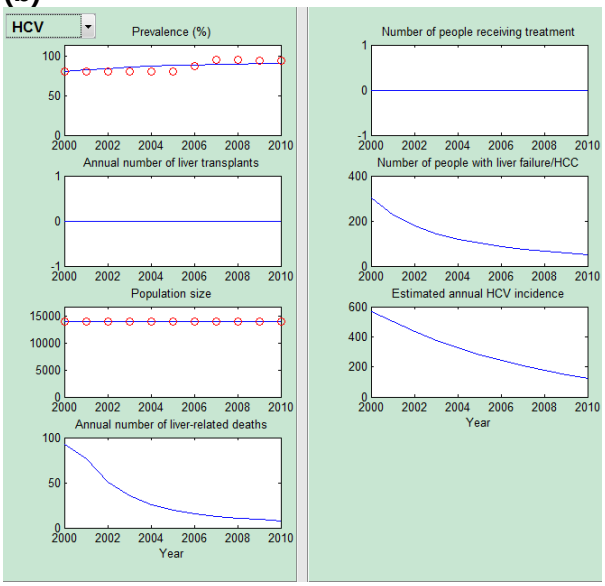


Estonia

(a)

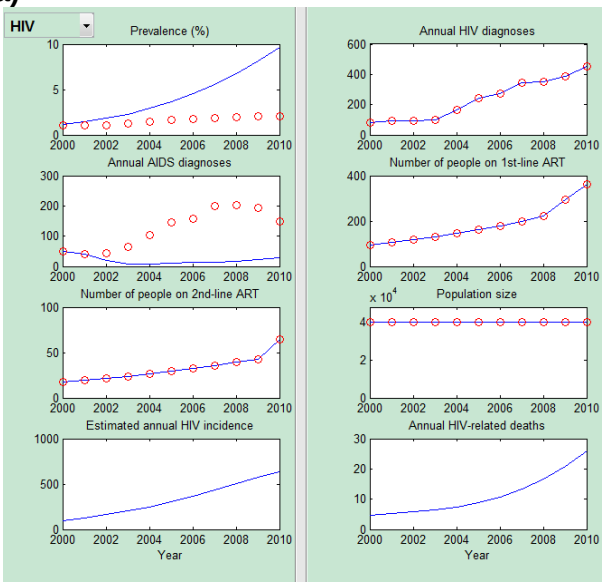


(b)



Georgia

(a)



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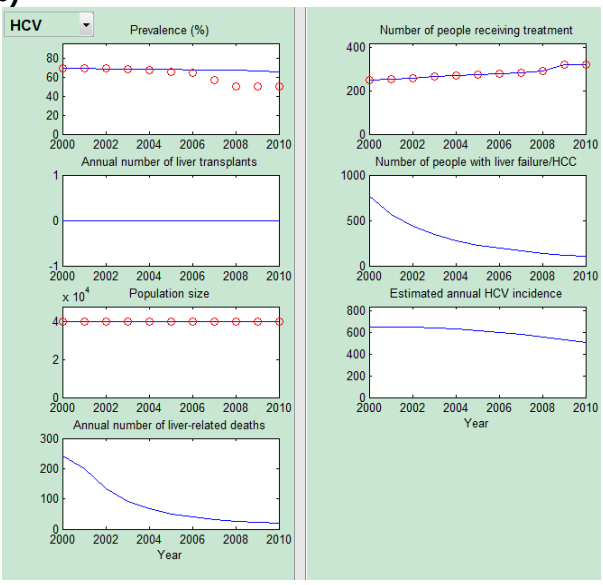
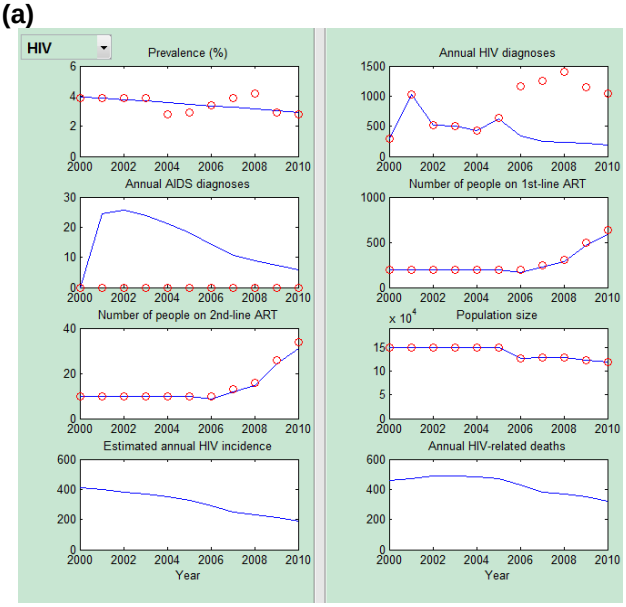


Kazakhstan

(a)



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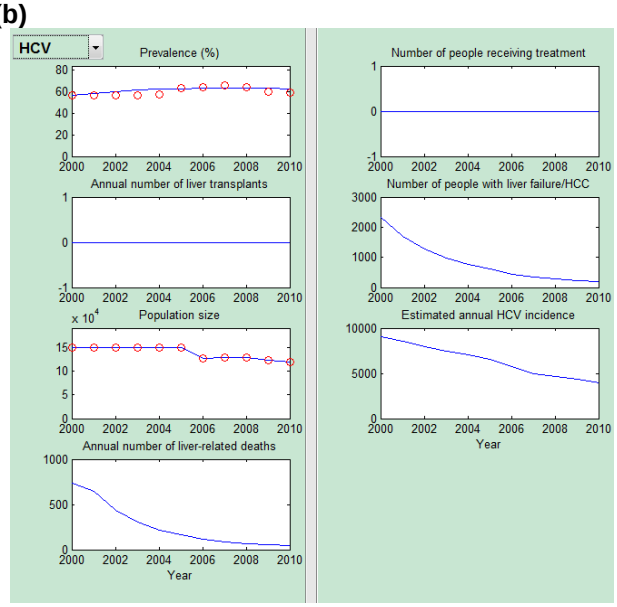
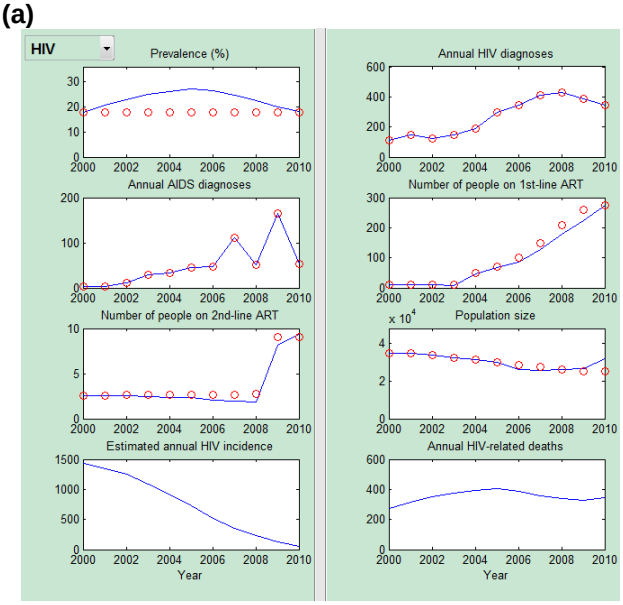


Moldova

(a)



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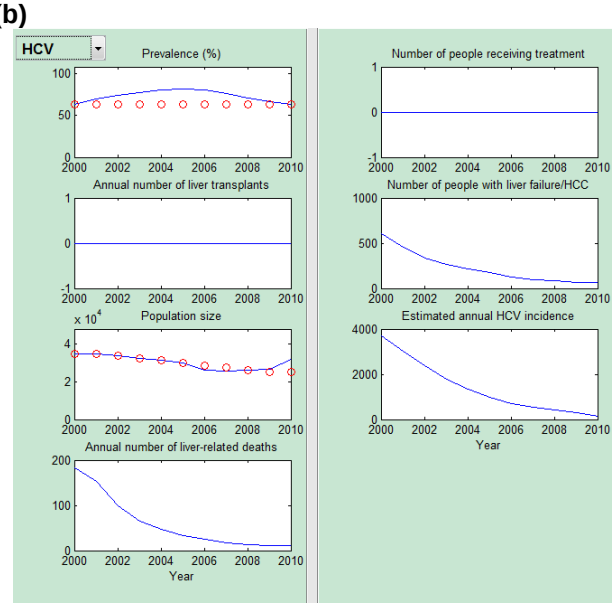
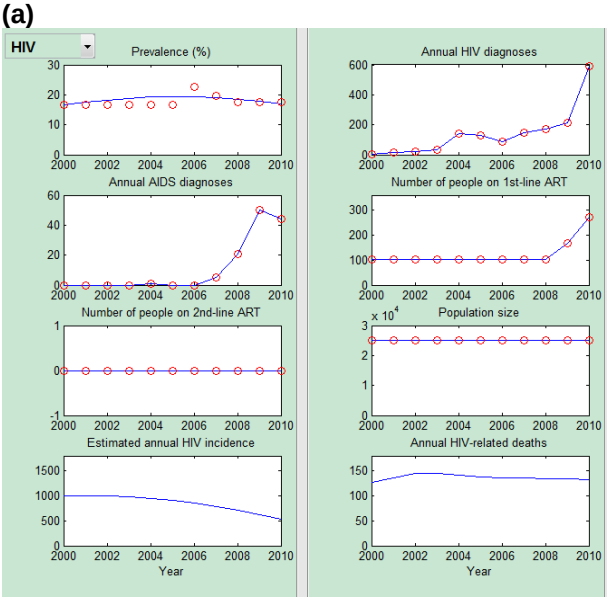


Tajikistan

(a)



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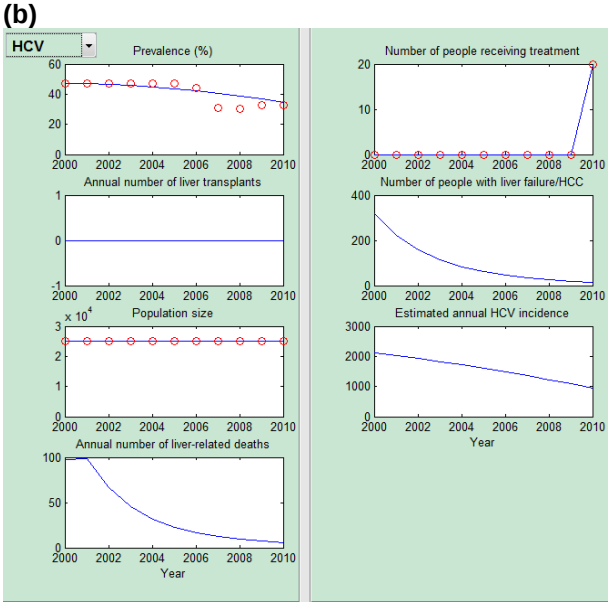
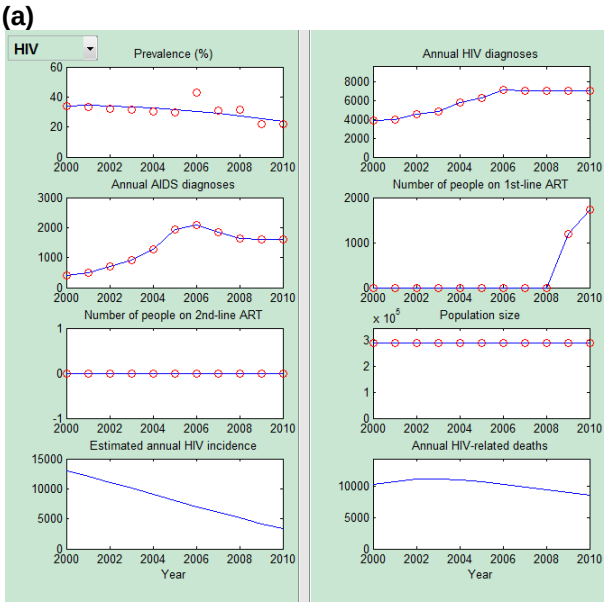


Ukraine

(a)



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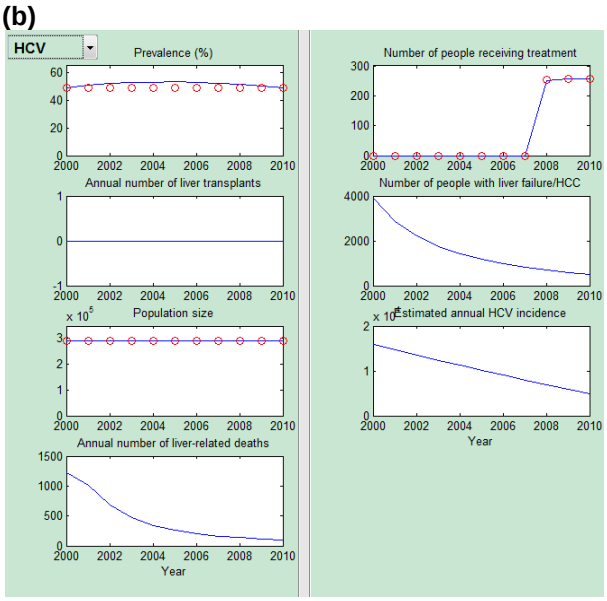
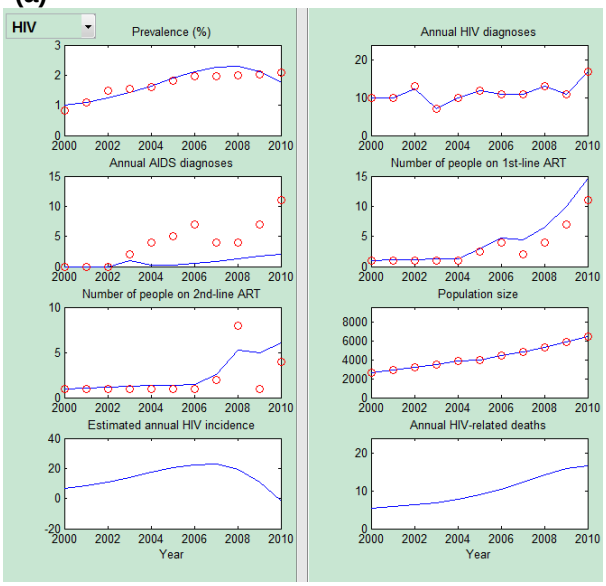


Russia-Kursk

(a)



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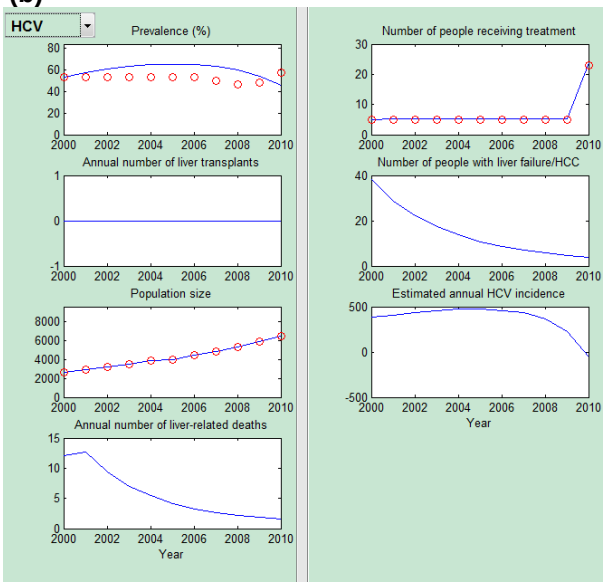

Russia-Lipetsk

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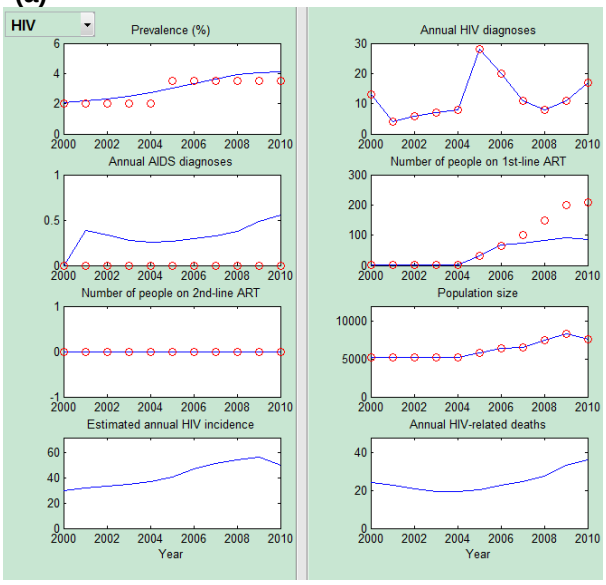

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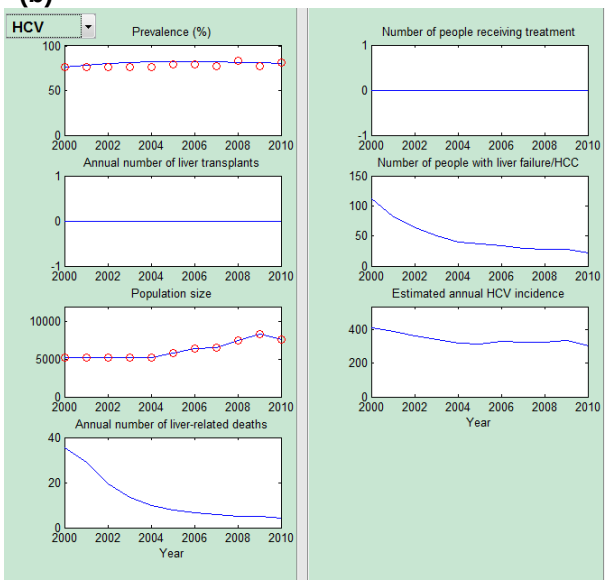
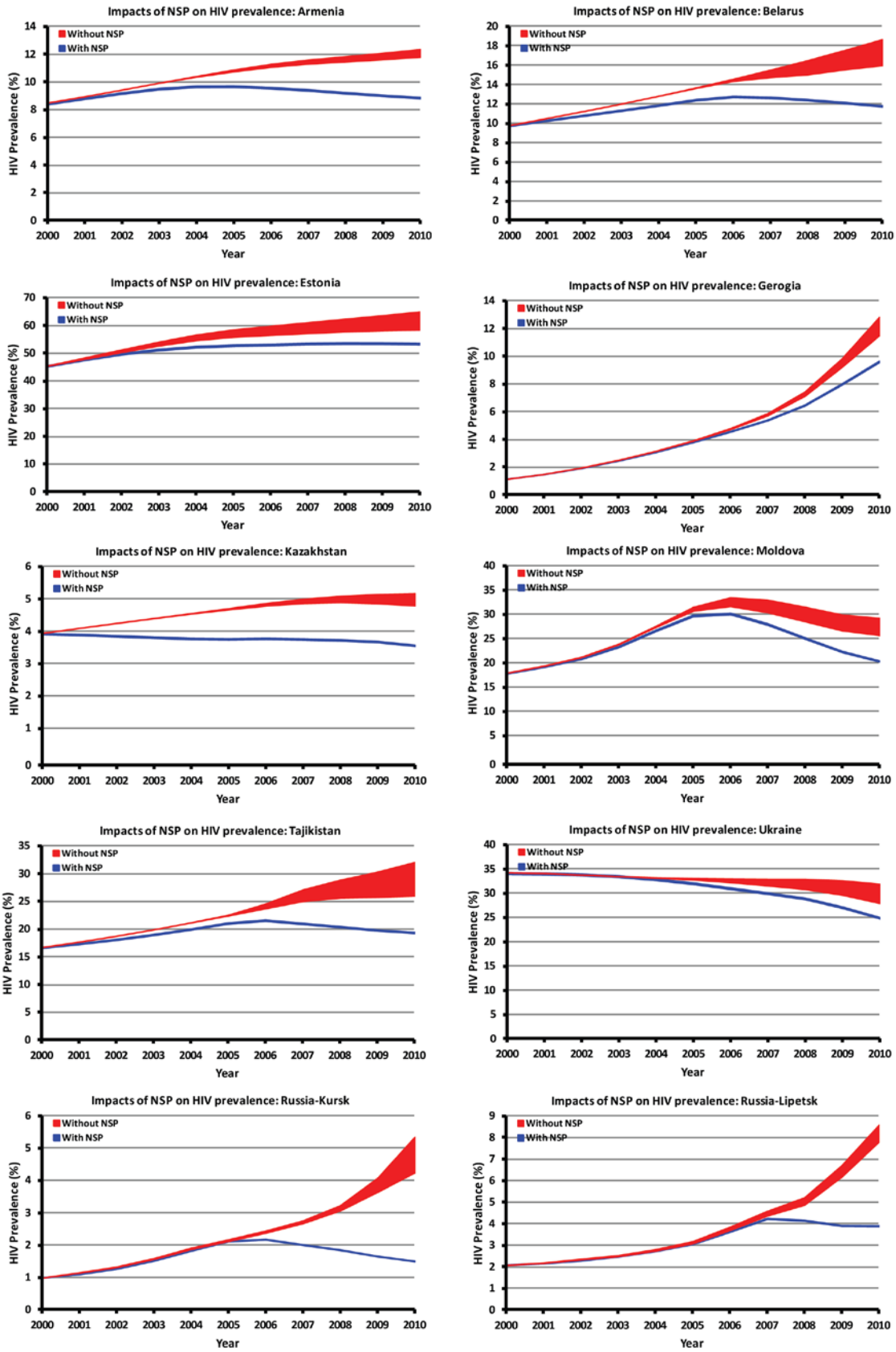


Model epidemic projections based on pre-NSP conditions

Prevention programs aim to reduce incidence of new infections. However, direct measures of incidence are not available in any of the case study countries; trends in prevalence are the only biological marker available. If rates of removal from the population (death, injecting cessation, migration) remain constant and incidence decreases then prevalence should also decrease. However, over the same timeframe that NSPs were scaled-up there were also increases in some other treatment and prevention programs. It should be noted that most other programs did not have large coverage among people who inject drugs. We aimed to determine what level of prevalence would be expected in the absence of NSPs (with pre-NSP syringe sharing behaviors) and ascertain whether observed prevalence levels among PWID were plausible without NSPs. The width of uncertainty bounds was dictated by the choice to use latin hypercube sampling over all parameter values and range of trajectories under different scenarios overlapped with observed data; however, when we considered only parameter sets which yielded trajectories that had ‘reasonable’ fits to the observed data then scenarios simulated without NSPs (but with other programs) deviated from the observed data.

Figure S5. Impacts of NSP on HIV prevalence in each country



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