Appendix: Description of the mathematical model, parameter values, cost data, and sensitivity analyses

Description of mathematical model

A mathematical model was developed to estimate HIV and HCV incidence and other disease outcomes. Our model tracks the population of people who inject drugs 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 due, by health state, over time. All parameter values were estimated based on published literature and available data from Australian reports and databases.

A schematic diagram of compartments in the HIV and HCV transmission model for inject drug users (IDUs) is presented in Figure 2 of the main manuscript. The change in the number of people in each compartment was tracked mathematically by formulating a system of ordinary differential equations. Twenty-one compartments represent IDUs 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; those who failed treatment may receive second-line treatment. The description of health states are shown in Table A.1. Twenty-two compartments represent IDUs 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 or hepatocellular carcinoma, or can 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. Coinfection is not considered in this model.

Table A.1: Number of compartments in HIV/HCV.

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)	

An ordinary differential equation (ODE) was developed to describe the change in the number of people in each of these compartmental health states over time; since there is one ODE for each compartment, there were 43 ODEs in total. The rate of change in the numbers of people in each compartment depends on the net rates of people entering and leaving the health state. Each ODE was mathematically described based on standard translation from the schematic diagram of the model presented in Figure 2 of the main manuscript [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:

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

where S is the number of uninfected active IDUs, 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 IDUs acquire infection.

The force of infection is the only rate between health states to be dependent on other health states (namely, numbers of people in the infected health states). To calculate the force of infection, we assume that each IDU 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:

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

Equations

HIV-infected individuals

Susceptible

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

Undiagnosed

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

$$\underbrace{\frac{dI^U_{350500}}{dt}}_{\text{Change in infecteds (350<CD4<500, Undiagnosed)}} = \underbrace{\tau_{500} I^U_{500}}_{\text{Progress from CD4>500}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\mu_{350500}}_{\text{HIV-related death (350<CD4<500)}} + \underbrace{\tau_{350500}}_{\text{Progress to 200<CD4<350}} + \underbrace{\eta_{350500}}_{\text{Testingrate (350<CD4<500)}} \right) I^U_{350500}$$

$$\underbrace{\frac{dI^U_{200350}}{dt}}_{\text{Change in infecteds (200<CD4<350, Undiagnosed)}} = \underbrace{\tau_{350500} I^U_{350500}}_{\text{Progress from 350<CD4<500}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\mu_{200350}}_{\text{HIV-related death (200<CD4<350)}} + \underbrace{\tau_{200350}}_{\text{Progress to CD4<200}} + \underbrace{\eta_{200350}}_{\text{Testing rate (200<CD4<350)}} \right) I^U_{200350}$$

$$\underbrace{\frac{dI^U_{200}}{dt}}_{\text{Change in infecteds (CD4<200, Undiagnosed)}} = \underbrace{\tau_{200350} I^U_{200350}}_{\text{Progress from 200<CD4<350}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\mu_{200}}_{\text{HIV-related death (CD4<200)}} + \underbrace{\eta_{200}}_{\text{Testing rate (CD4<200)}} \right) I^U_{200}$$

Diagnosed

$$\underbrace{\frac{dI^{D}_{500}}{dt}}_{\text{Change in infecteds (CD4>500, diagnosed)}} = \overbrace{\eta_{500} I^{U}_{500}}^{\text{Diagnosed (CD4>500)}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_{D}}_{\text{Drug-related death}} + \underbrace{\mu_{500}}_{\text{HIV-related death (CD4>500)}} + \underbrace{\tau_{500}}_{\text{Progress to 350<CD4<500}} + \overbrace{\sigma_{500}}^{\text{Commence 1stline treatment (CD4>500)}} \right) I^{D}_{500}$$

$$\underbrace{\frac{dI^{D}_{350500}}{dt}}_{\text{Change in infecteds (350<CD4<500, diagnosed)}} = \overbrace{\tau_{500} I^{D}_{500}}^{\text{Progress from CD4>500}} + \overbrace{\eta_{350500} I^{U}_{350500}}^{\text{Diagnosed (350<CD4<500)}}$$

$$- \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_{D}}_{\text{Drug-related death}} + \overbrace{\mu_{350500}}^{\text{HIV-related death (350<CD4<500)}} + \overbrace{\tau_{350500}}^{\text{Progress to 200<CD4<350}} + \overbrace{\sigma_{350500}}^{\text{Commence 1stline treatment (350<CD4<500)}} \right) I^{D}_{350500}$$

$$\underbrace{\frac{dI^{D}_{200350}}{dt}}_{\text{Change in infecteds (200<CD4<350, diagnosed)}} = \overbrace{\tau_{350500} I^{D}_{350500}}^{\text{Progress from 350<CD4<500}} + \overbrace{\eta_{200350} I^{U}_{200350}}^{\text{Diagnosed (200<CD4<350)}}$$

$$- \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_{D}}_{\text{Drug-related death}} + \overbrace{\mu_{200350}}^{\text{HIV-related death (200<CD4<350)}} + \overbrace{\tau_{200350}}^{\text{Progress to CD4<200}} + \overbrace{\sigma_{200350}}^{\text{Commence 1stline treatment (200<CD4<350)}} \right) I^{D}_{200350}$$

$$\underbrace{\frac{dI^{D}_{200}}{dt}}_{\text{Change in infecteds (CD4<200, diagnosed)}} = \overbrace{\tau_{200350} I^{D}_{200350}}^{\text{Progress from 200<CD4<350}} + \overbrace{\eta_{200} I^{U}_{200}}^{\text{Diagnosed (CD4<200)}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_{D}}_{\text{Drug-related death}} + \underbrace{\mu_{200}}_{\text{HIV-related death (CD4<200)}} + \overbrace{\sigma_{200}}^{\text{Commence 1stline treatment (CD4<200)}} \right) I^{D}_{200}$$

First-line treatment

$$\overbrace{\frac{dI_{500_{1st}}}{dt}}^{\substack{\text{Change in infecteds (CD4>500)}\\ \text{during 1st treatment}}} = \overbrace{\sigma_{500} I_{500}^{D}}^{\substack{\text{Commenced 1st line}\\ \text{therapy (CD4>500)}}} + \overbrace{\omega_{350500} I_{350500_{1st}}}^{\substack{\text{Viral supression}\\ \text{during 1st line therapy}\\ \text{(350<CD4<500)}}} - \left(\overbrace{\mu}^{\substack{\text{Background}\\ \text{death}}} + \overbrace{\mu_D}^{\substack{\text{Drug-related}\\ \text{death}}} + \overbrace{\mu_T}^{\substack{\text{HIV-related}\\ \text{death}\\ \text{(on ART)}}} + \overbrace{\phi_{500}}^{\substack{\text{Viral rebound}\\ \text{(CD4>500)}}} \right) I_{500_{1st}}$$

$$\overbrace{\frac{dI_{350500_{1st}}}{dt}}^{\substack{\text{Change in infecteds (350<CD4<500)}\\ \text{during 1st treatment}}} = \overbrace{\sigma_{350500} I_{350500}^{D}}^{\substack{\text{Commenced 1st line}\\ \text{therapy}\\ \text{(350<CD4<500)}}} + \overbrace{\omega_{200350} I_{200350_{1st}}}^{\substack{\text{Viral supression}\\ \text{during 1st line therapy}\\ \text{(200<CD4<350)}}}$$

$$- \left(\overbrace{\mu}^{\substack{\text{Background}\\ \text{death}}} + \overbrace{\mu_D}^{\substack{\text{Drug-related}\\ \text{death}}} + \overbrace{\mu_T}^{\substack{\text{HIV-related}\\ \text{death}\\ \text{(on ART)}}} + \overbrace{\phi_{350500}}^{\substack{\text{Viral rebound}\\ \text{(350<CD4<500)}}} + \overbrace{\omega_{350500}}^{\substack{\text{Viral supression}\\ \text{(350<CD4<500)}}} \right) I_{350500_{1st}}$$

$$\overbrace{\frac{dI_{200350_{1st}}}{dt}}^{\substack{\text{Change in infecteds (200<CD4<350)}\\ \text{during 1st treatment}}} = \overbrace{\sigma_{200350} I_{200350}^{D}}^{\substack{\text{Commenced 1st line}\\ \text{therapy (200<CD4<350)}}} + \overbrace{\omega_{200} I_{200_{1st}}}^{\substack{\text{Viral supression}\\ \text{during 1st line therapy}\\ \text{(CD4<200)}}}$$

$$- \left(\overbrace{\mu}^{\substack{\text{Background}\\ \text{death}}} + \overbrace{\mu_D}^{\substack{\text{Drug-related}\\ \text{death}}} + \overbrace{\mu_T}^{\substack{\text{HIV-related}\\ \text{death}\\ \text{(on ART)}}} + \overbrace{\phi_{200350}}^{\substack{\text{Viral rebound}\\ \text{(200<CD4<350)}}} + \overbrace{\omega_{200350}}^{\substack{\text{Viral supression}\\ \text{(200<CD4<350)}}} \right) I_{200350_{1st}}$$

$$\overbrace{\frac{dI_{200_{1st}}}{dt}}^{\substack{\text{Change in infecteds (CD4<200)}\\ \text{during 1st treatment}}} = \overbrace{\sigma_{200} I_{200}^{D}}^{\substack{\text{Commenced 1st line}\\ \text{therapy (CD4<200)}}}$$

$$- \left(\overbrace{\mu}^{\substack{\text{Background}\\ \text{death}}} + \overbrace{\mu_D}^{\substack{\text{Drug-related}\\ \text{death}}} + \overbrace{\mu_T}^{\substack{\text{HIV-related}\\ \text{death}\\ \text{(on ART)}}} + \overbrace{\phi_{200}}^{\substack{\text{Viral rebound}\\ \text{(CD4<200)}}} + \overbrace{\omega_{200}}^{\substack{\text{Viral supression}\\ \text{(CD4<200)}}} \right) I_{200_{1st}}$$

Treatment failure

$$\overbrace{\frac{dI_{500_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (CD4>500)}} = \overbrace{\phi_{500} I_{500_{1st}}}^{\text{Viral rebound during 1st line therapy (CD4>500)}} + \overbrace{\phi^{S}_{500} I_{500_{2nd}}}^{\text{Viral rebound during 2nd line therapy (CD4>500)}}$$
$$- \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\mu_T}^{\text{HIV-related death (on ART)}} + \overbrace{\tau^{F}_{500}}^{\text{Progress to (350<CD4<500)}} + \overbrace{\delta_{500}}^{\text{Commence 2nd line therapy (CD4>500)}} \right) I_{500_{Fail}}$$

$$\overbrace{\frac{dI_{350500_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (350<CD4<500)}} = \overbrace{\phi_{350500} I_{350500_{1st}}}^{\text{Viral rebound during 1st line therapy (350<CD4<500)}} + \overbrace{\phi^{S}_{350500} I_{350500_{2nd}}}^{\text{Viral rebound during 2nd line therapy (350<CD4<500)}} + \overbrace{\tau^{F}_{500} I_{500_{Fail}}}^{\text{Progress from CD4>500 after 1st line treatment failure}}$$
$$- \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\mu_T}^{\text{HIV-related death (on ART)}} + \overbrace{\tau^{F}_{350500}}^{\text{Progress to (200<CD4<350)}} + \overbrace{\delta_{350500}}^{\text{Commence 2nd line therapy (350<CD4<500)}} \right) I_{350500_{Fail}}$$

$$\overbrace{\frac{dI_{200350_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (200<CD4<350)}} = \overbrace{\phi_{200350} I_{200350_{1st}}}^{\text{Viral rebound during 1st line therapy (200<CD4<350)}} + \overbrace{\phi^{S}_{200350} I_{200350_{2nd}}}^{\text{Viral rebound during 2nd line therapy (200<CD4<350)}} + \overbrace{\tau^{F}_{350500} I_{350500_{Fail}}}^{\text{Progress from 350<CD4<500 after treatment failure}}$$
$$- \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\mu_T}^{\text{HIV-related death (on ART)}} + \overbrace{\tau^{F}_{200350}}^{\text{Progress to CD4<200}} + \overbrace{\sigma_{200350}}^{\text{Commence 2nd line therapy (200<CD4<350)}} \right) I_{200350_{Fail}}$$

$$\overbrace{\frac{dI_{200_{Fail}}}{dt}}^{\text{Change in treatment failure infecteds (CD4<200)}} = \overbrace{\phi_{200} I_{200_{1st}}}^{\text{Viral rebound during 1st line therapy (CD4<200)}} + \overbrace{\phi^{S}_{200} I_{200_{2nd}}}^{\text{Viral rebound during 2nd line therapy (CD4<200)}} + \overbrace{\tau^{F}_{200350} I_{200350_{Fail}}}^{\text{Progress from 200<CD4<350 after treatment failure}}$$
$$- \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\mu_T}^{\text{HIV-related death (on ART)}} + \overbrace{\sigma_{200}}^{\text{Commence 2nd line therapy (CD4<200)}} \right) I_{200_{Fail}}$$

Second-line treatment

$$\overbrace{\frac{dI_{500_{2nd}}}{dt}}^{\substack{\text{Change in}\\ \text{infecteds (CD4>500)}\\ \text{on 2nd line treatment}}} = \overbrace{\delta_{500} I_{500_{Fail}}}^{\substack{\text{Commence 2nd line}\\ \text{therapy (CD4>500)}}} + \overbrace{\omega_{350500} I_{35000_{2nd}}}^{\substack{\text{Viral supression}\\ \text{during 2nd line therapy}\\ \text{from 350<CD4<500}}}$$

$$- \left(\overbrace{\mu}^{\substack{\text{Background}\\ \text{death}}} + \overbrace{\mu_D}^{\substack{\text{Drug-related}\\ \text{death}}} + \overbrace{\mu_T}^{\substack{\text{HIV-related}\\ \text{death (on ART)}}} + \overbrace{\phi^S_{500}}^{\substack{\text{Viral rebound during}\\ \text{2nd line therapy}\\ \text{(CD4>500)}}} \right) I_{500_{2nd}}$$

$$\overbrace{\frac{dI_{350500_{2nd}}}{dt}}^{\substack{\text{Change in}\\ \text{infecteds (350<CD4<500)}\\ \text{on 2nd line treatment}}} = \overbrace{\delta_{350500} I_{350500_{Fail}}}^{\substack{\text{Commence 2nd line}\\ \text{therapy}\\ \text{(350<CD4<500)}}} + \overbrace{\omega_{200350} I_{200350_{2nd}}}^{\substack{\text{Viral supression}\\ \text{during 2nd line therapy}\\ \text{from 200<CD4<350}}}$$

$$- \left(\overbrace{\mu}^{\substack{\text{Background}\\ \text{death}}} + \overbrace{\mu_D}^{\substack{\text{Drug-related}\\ \text{death}}} + \overbrace{\mu_T}^{\substack{\text{HIV-related}\\ \text{death}\\ \text{(on ART)}}} + \overbrace{\phi^S_{350500}}^{\substack{\text{Viral rebound during}\\ \text{2nd line therapy}\\ \text{(350<CD4<500)}}} + \overbrace{\omega_{350500}}^{\substack{\text{Viral supression}\\ \text{(350<CD4<500)}}} \right) I_{350500_{2nd}}$$

$$\overbrace{\frac{dI_{200350_{2nd}}}{dt}}^{\text{Change in infecteds (200<CD4<350) on 2nd line treatment}} = \overbrace{\delta_{200350} I_{200350_{Fail}}}^{\text{Commence 2nd line therapy (200<CD4<350)}} + \overbrace{\omega_{200} I_{200_{2nd}}}^{\text{Viral supression during 2nd line therapy from CD4<200}}$$

$$- \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\mu_T}^{\text{HIV-related death (on ART)}} + \overbrace{\phi^S_{200350}}^{\text{Viral rebound during 2nd line therapy (200<CD4<350)}} + \overbrace{\omega_{200350}}^{\text{Viral supression (200<CD4<350)}} \right) I_{200350_{2nd}}$$

$$\overbrace{\frac{dI_{200_{2nd}}}{dt}}^{\text{Change in infecteds (CD4<200) on 2nd treatment}} = \overbrace{\sigma_{200} I_{200_{Fail}}}^{\text{Commence 2nd line therapy (CD4<200)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{\mu_T}^{\text{HIV-related death (on ART)}} + \overbrace{\phi^S_{200}}^{\text{Viral rebound during 2nd line therapy (CD4<200)}} + \overbrace{\omega_{200}}^{\text{Viral supression (CD4<200)}} \right) I_{200_{2nd}}$$

HCV-infected individuals

Susceptible

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

Undiagnosed

$$\underbrace{\frac{dI_A^U}{dt}}_{\text{Change in acute infecteds}} = \underbrace{\lambda_{HCV} S}_{\text{New infections}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\psi}_{\text{Spontaneous clearance of HCV}} + \underbrace{\tau_A}_{\text{Progress to F0}} + \underbrace{\sigma_A}_{\text{Testing rate (acute)}} \right) I_A^U$$

$$\underbrace{\frac{dI_{F0}^U}{dt}}_{\text{Change in F0 infecteds}} = \underbrace{\tau_A I_A^U}_{\text{Progress from acute}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\sigma_{F0}}_{\text{Testing rate (F0)}} + \underbrace{\tau_{F0}}_{\text{Progress to F1}} \right) I_{F0}^U$$

$$\underbrace{\frac{dI_{F1}^U}{dt}}_{\text{Change in F1 infecteds}} = \underbrace{\overbrace{\tau_{F0} I_{F0}^U}^{\text{Progress from F0}}}_{} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\sigma_{F1}}_{\text{Testing rate (F1)}} + \underbrace{\tau_{F1}}_{\text{Progress to F2}} \right) I_{F1}^U$$

$$\underbrace{\frac{dI_{F2}^U}{dt}}_{\text{Change in F2 infecteds}} = \underbrace{\tau_{F1} I_{F1}^U}_{\text{Progress from F1}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\sigma_{F2}}_{\text{Testing rate (F2)}} + \underbrace{\tau_{F2}}_{\text{Progress to F3}} \right) I_{F2}^U$$

$$\underbrace{\frac{dI_{F3}}{dt}}_{\substack{\text{Change in}\\ \text{F3 infecteds}}} = \underbrace{\tau_{F2} I_{F2}^{U}}_{\substack{\text{Progress from}\\ F2}} - \left(\underbrace{\mu}_{\substack{\text{Background}\\ \text{death}}} + \underbrace{\mu_D}_{\substack{\text{Drug-related}\\ \text{death}}} + \underbrace{\sigma_{F3}}_{\substack{\text{Testingrate}\\ (F3)}} + \underbrace{\tau_{F3}}_{\substack{\text{Progress to}\\ F4}} \right) I_{F3}^{U}$$

$$\underbrace{\frac{dI_{F4}^{U}}{dt}}_{\substack{\text{Change in}\\ \text{F4 infecteds}}} = \underbrace{\tau_{F3} I_{F3}^{U}}_{\substack{\text{Progress from}\\ F3}} - \left(\underbrace{\mu}_{\substack{\text{Background}\\ \text{death}}} + \underbrace{\mu_D}_{\substack{\text{Drug-related}\\ \text{death}}} + \underbrace{\sigma_{F4}}_{\substack{\text{Testingrate}\\ (F4)}} + \underbrace{\tau_{F4LF}}_{\substack{\text{Progress to}\\ \text{liver failure}}} + \underbrace{\tau_{F4HCC}}_{\substack{\text{Progress to}\\ HCC}} \right) I_{F4}^{U}$$

Diagnosed

$$\underbrace{\frac{dI_{A}^{D}}{dt}}_{\substack{\text{Change in}\\ \text{acute infecteds}}} = \underbrace{\sigma_A I_A^U}_{\substack{\text{Diagnosed}\\ (\text{acute})}} + \underbrace{\left(1-\gamma_A\right)\nu_A I_A^T}_{\substack{\text{Cease treatment}\\ (\text{acute})}} - \left(\underbrace{\mu}_{\substack{\text{Background}\\ \text{death}}} + \underbrace{\mu_D}_{\substack{\text{Drug-related}\\ \text{death}}} + \underbrace{\psi}_{\substack{\text{Spontaneous}\\ \text{clearance of HCV}}} + \underbrace{\tau_A}_{\substack{\text{Progress to}\\ F0}} + \underbrace{\eta_A}_{\substack{\text{Commence}\\ \text{treatment (acute)}}} \right) I_A^D$$

$$\underbrace{\frac{dI_{F0}^{D}}{dt}}_{\substack{\text{Change in}\\ \text{acute infecteds}}} = \underbrace{\sigma_{F0} I_{F0}^{U}}_{\substack{\text{Diagnosed}\\ (F0)}} + \underbrace{\left(1-\gamma_{F0}\right)\nu_F I_F^T}_{\substack{\text{Cease treatment}\\ (F0)}} - \left(\underbrace{\mu}_{\substack{\text{Background}\\ \text{death}}} + \underbrace{\mu_D}_{\substack{\text{Drug-related}\\ \text{death}}} + \underbrace{\tau_{F0}}_{\substack{\text{Progress to}\\ F1}} + \underbrace{\eta_{F0}}_{\substack{\text{Commence}\\ \text{treatment (F0)}}} \right) I_{F0}^{D}$$

$$\frac{dI_{F1}^{D}}{dt} = \overbrace{\sigma_{F1} I_{F1}^{U}}^{\substack{\text{Change in F1 infecteds} \\ \text{Diagnosed (F0)}}} + \overbrace{\tau_{F0} I_{F0}^{D}}^{\text{Progress from F0}} + \overbrace{(1-\gamma_F)\nu_F I_{F1}^{T}}^{\text{Cease treatment (F1)}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\eta_{F1}}_{\text{Commence treatment (F1)}} + \overbrace{\tau_{F1}}^{\text{Progress to F2}} \right) I_{F1}^{D}$$

$$\frac{dI_{F2}^{D}}{dt} = \overbrace{\sigma_{F2} I_{F2}^{U}}^{\substack{\text{Change in F2 infecteds} \\ \text{Diagnosed (F2)}}} + \overbrace{\tau_{F1} I_{F1}^{D}}^{\text{Progress from F1}} + \overbrace{(1-\gamma_F)\nu_F I_{F2}^{T}}^{\text{Cease treatment (F2)}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\eta_{F2}}_{\text{Commence treatment (F2)}} + \overbrace{\tau_{F2}}^{\text{Progress to F3}} \right) I_{F2}^{D}$$

$$\frac{dI_{F3}^{D}}{dt} = \overbrace{\sigma_{F3} I_{F3}^{U}}^{\substack{\text{Change in F3 infecteds} \\ \text{Diagnosed (F3)}}} + \overbrace{\tau_{F2} I_{F2}^{D}}^{\text{Progress from F2}} + \overbrace{(1-\gamma_F)\nu_F I_{F3}^{T}}^{\text{Cease treatment (F3)}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\eta_{F3}}_{\text{Commence treatment (F3)}} + \overbrace{\tau_{F3}}^{\text{Progress to F4}} \right) I_{F3}^{D}$$

$$\frac{dI_{F4}^{D}}{dt} = \overbrace{\sigma_{F4} I_{F4}^{U}}^{\substack{\text{Change in F4 infecteds} \\ \text{Diagnosed (F4)}}} + \overbrace{\tau_{F3} I_{F3}^{D}}^{\text{Progress from F3}} + \overbrace{(1-\gamma_F)\nu_F I_{F4}^{T}}^{\text{Cease treatment (F4)}} - \left(\underbrace{\mu}_{\text{Background death}} + \underbrace{\mu_D}_{\text{Drug-related death}} + \underbrace{\eta_{F4}}_{\text{Commence treatment (F3)}} + \overbrace{\tau_{F4LF}}^{\text{Progress to liver failure}} + \overbrace{\tau_{F4HCC}}^{\text{Progress to HCC}} \right) I_{F4}^{D}$$

Receiving HCV treatment

Change in acute infecteds on treatment

$$\frac{dI_A^T}{dt} = \overbrace{\eta_A I_A^D}^{\text{Commenced treatment (acute)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{(1-\gamma_A)\nu_A}^{\text{Cease treatment (F4)}} + \overbrace{\gamma_A \nu_A}^{\text{Viral clearance on treatment (acute)}} + \overbrace{\tau_A^T}^{\text{Progress to F0 during treatment}} \right) I_A^T$$

Change in F0 infecteds on treatment

$$\frac{dI_{F0}^T}{dt} = \overbrace{\tau_A^T I_A^T}^{\text{Progress from acute during treatment}} + \overbrace{\eta_{F0} I_{F0}^D}^{\text{Commenced treatment (F0)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{(1-\gamma_{F0})\nu_F}^{\text{Cease treatment (F0)}} + \overbrace{\gamma_{F0}\nu_F}^{\text{Viral clearance on treatment (F0)}} + \overbrace{\tau_{F0}^T}^{\text{Progress to F1 during treatment}} \right) I_{F0}^T$$

Change in F1 infecteds on treatment

$$\frac{dI_{F1}^T}{dt} = \overbrace{\tau_{F0}^T I_{F0}^T}^{\text{Progress from F0 during treatment}} + \overbrace{\eta_{F1} I_{F1}^D}^{\text{Commenced treatment (F1)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{(1-\gamma_F)\nu_F^M}^{\text{Cease treatment (F1)}} + \overbrace{\gamma_F^M \nu_F^M}^{\text{Viral clearance on treatment (F1)}} + \overbrace{\tau_{F1}^T}^{\text{Progress to F2 during treatment}} \right) I_{F1}^T$$

Change in F2 infecteds on treatment

$$\frac{dI_{F2}^T}{dt} = \overbrace{\tau_{F1}^T I_{F1}^T}^{\text{Progress from F1 during treatment}} + \overbrace{\eta_{F2} I_{F2}^D}^{\text{Commenced treatment (F2)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{(1-\gamma_F)\nu_F}^{\text{Cease treatment (F2)}} + \overbrace{\gamma_F \nu_F}^{\text{Viral clearance on treatment (F2)}} + \overbrace{\tau_{F2}^T}^{\text{Progress to F3 during treatment}} \right) I_{F2}^T$$

Change in F3 infecteds on treatment

$$\frac{dI_{F3}^{T}}{dt} = \overbrace{\tau_{F2}^{T} I_{F2}^{T}}^{\text{Progress from F2 during treatment}} + \overbrace{\eta_{F3} I_{F3}^{D}}^{\text{Commenced treatment (F3)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{(1-\gamma_F)\nu_F}^{\text{Cease treatment (F3)}} + \overbrace{\gamma_F \nu_F}^{\text{Viral clearance on treatment (F3)}} + \overbrace{\tau_{F3}^{T}}^{\text{Progress to F4 during treatment}} \right) I_{F3}^{T}$$

Change in F4 infecteds on treatment

$$\frac{dI_{F4}^{T}}{dt} = \overbrace{\tau_{F3}^{T} I_{F3}^{T}}^{\text{Progress from F3 during treatment}} + \overbrace{\eta_{F4} I_{F4}^{D}}^{\text{Commenced treatment (F4)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_D}^{\text{Drug-related death}} + \overbrace{(1-\gamma_F)\nu_F}^{\text{Cease treatment (F4)}} + \overbrace{\gamma_F \nu_F}^{\text{Viral clearance on treatment (F4)}} \right) I_{F4}^{T}$$

Change in liver failure infecteds

$$\frac{dI_{LF}}{dt} = \overbrace{\tau_{F4LF} I_{F4}^{U}}^{\text{Progress from F4 (undiagnosed)}} + \overbrace{\tau_{F4LF} I_{F4}^{D}}^{\text{Progress from F4 (diagnosed)}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{LF}}^{\text{Liver failure related death}} + \overbrace{\tau_{LFHCC}}^{\text{Progress to HCC}} + \overbrace{\tau_{LFLT}}^{\text{Progress to LT}} \right) I_{LF}$$

Change in HCC infecteds

$$\frac{dI_{HCC}}{dt} = \overbrace{\tau_{F4HCC} I_{F4}^{U}}^{\text{Progress from F4 (undiagnosed)}} + \overbrace{\tau_{F4HCC} I_{F4}^{D}}^{\text{Progress from F4 (diagnosed)}} + \overbrace{\tau_{LFHCC} I_{LF}}^{\text{Progress from LF}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{HCC}}^{\text{HCC related death}} + \overbrace{\tau_{HCCLT}}^{\text{Progress to LT}} \right) I_{HCC}$$

Change in Liver transplants

$$\frac{dI_{LT}}{dt} = \overbrace{\tau_{LFLT} I_{LF}}^{\text{Progress from liver failure}} + \overbrace{\tau_{HCCLT} I_{HCC}}^{\text{Progress from HCC}} - \left(\overbrace{\mu}^{\text{Background death}} + \overbrace{\mu_{LT}}^{\text{Liver transplant related death}} \right) I_{LT}$$

Model parameters

Table A.1: Model parameters related to HIV

Symbol	Description	Values	References
Transmission			
β_{HIV}	Transmission probability of HIV per injection with a contaminated syringe	0.6-0.8%	[2, 3], a
r	Effectiveness of ART	50-80%	[4-10]
Testing rate			
η	Proportion of individuals that received HIV test every year	48-66%	[11]
Disease progression of individuals without treatment			
$1/\tau_{CD4>500}$	Average time for HIV-infected individuals to progress from CD4 count **>500** to CD4 count **350-500**	4.09 (3.79-4.42) years	[12], b
$1/\tau_{350<CD4<500}$	Average time for 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 HIV-infected individuals to progress from CD4 count **200-350** to CD4 count **<200**	1.96 (1.81-2.13) years	
Disease progression on treatment (viral suppression)			
$1/\omega^{U}_{CD4<200}$	Average time for HIV infected individuals **on ART** to progress from CD4 count **<200** to CD4 count **200-350**	2.80 (2.33-3.58) years	[13] , c
$1/\omega^{U}_{200<CD4<350}$	Average time for HIV infected individuals **on ART** 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** to progress from CD4 count **350-500** to CD4 count **>500**	2.20 (1.07-7.28) years	
Commencement of treatment			
$\sigma_{CD4>500}$	Proportion of individuals with CD4 count **>500** that commence treatment for HIV each year	0.2	Experimental variable
$\sigma_{350<CD4<500}$	Proportion of individuals with CD4 count **350-500** that commence treatment for HIV each year	0.5	

$\sigma_{200<CD4<350}$	Proportion of individuals with CD4 count **200-350** that commence treatment for HIV each year	0.75-0.85	
$\sigma_{CD4<200}$	Proportion of individuals with **CD4** count **<200** that commence treatment for HIV each year	0.85-0.95	
Stopping treatment			
ϕ_S	Percentage of individuals on ART who cease therapy each year	1-5%	d
Response to treatment			
ϕ	Percentage of individuals on ART to experience viral rebound per year	3-6%	[14]
Response to treatment			
$1/\delta_{200<CD4<350}$	Average time after treatment failure for individuals with CD4 count **> 200** to go on second line ART	6-18 months	Experimental variable
$1/\delta_{CD4<200}$	Average time for individuals on ART with CD4 count **<200** to go on second-line ART	2-3 months	
Mortality Rates			
$\mu_{CD4>500}$	HIV-related death rate for patients with CD4 count >500 cells per µL	0.051% (0.035-0.068%)	[15]
$\mu_{350<CD4<500}$	HIV-related death rate for patients with CD4 count 350-500 cells per µL	0.128% (0.092-0.164%)	[15]
$\mu_{200<CD4<350}$	HIV-related death rate per 100 person-years for patients with CD4 count 200-350 cells per µL	1.0% (0.2-2.0)%	[15, 16]
$\mu_{CD4<200}$	HIV-related death rate per 100 person-years for patients with CD4 count <200 cells per µL	4.08 (0.30-7.86)%	

a Numerous studies have estimated the transmission risk of HIV in an occupational setting due to needlestick injury [17-23]. A model-based analysis evaluating population-level data in New Haven estimated the risk as ~0.7% [24]. Few studies have directly estimated the probability of HIV transmission per injection by IDUs using a contaminated syringe. In a long-term cohort study among injecting drug users in Bangkok, Thailand, a probability of transmission per exposure with a contaminated syringe was estimated to be 0.6% (0.4-0.9%) [3]. A review and meta-analysis suggested that the probability of transmission following a needlestick exposure is 0.23% (0-0.46%) and the infectivity per intravenous drug injection had a median of 0.8% (ranging 0.63%-2.4%) [2]. Estimates from studies based on occupational exposure tend to have lower transmission risk than estimates of risk by intravenous drug injection. Based on the injecting drug studies, we assume that the probability of transmission per drug-injection with a contaminated syringe ranges 0.6-0.8%.

b A summary of the relation between HIV-1 RNA concentration and decline in $CD4^+$ count from the prospective study by Mellors et al. [12] is given below:

Plasma HIV-1 RNA concentration (*copies/mL*)	**Mean decrease in $CD4^+$ T cell count per year (*cells/µL*)**
≤ 500	-36.3 (-30□□,-42.3)
501-3,000	-44.8 (-39.1,-50.5)
3,001-10,000	-55.2 (-50.7,-59.□)
10,001-30,000	-64.8 (-59.6,-70□0)

> 30,000	-76.5 (-70.5,-82.9)

With this data, and assuming that the average viral load is ~$10^{4.87}$ copies per mL for people without treatment, the $CD4^+$ T cell count decreases by an average of 76.5 (70.5, 82.9) every year.

To progress through the >500 CD4 cell category, we assume that the average CD4 count is 800 cells/μL after the 2-month acute phase of HIV infection and then declines at the constant rate of 76.5 (70.5, 82.9) cells/μL each year. Then the average time to progress through this compartment is 2/12 + 300/(76.5 (70.5, 82.9)) years; that is 4.09 (3.79, 4.42) years.

To progress through the 350-500 and 200-350 CD4 cell categories, we assume an average loss of 150 CD4 cells. Then the average time to progress through this compartment is 150/(76.5 (70.5, 82.9)) years; that is 1.96 (1.81, 2.13) years.

c

Below is a summary of data from [25] for changes in CD4 count over time among people who are on effective cART.

CD4 count at initiation of cART (cells per μL)	**Time since starting cART (years)**	**Current CD4 (cells per μL) means (95% CI)**
≤200	<1	76 (53-99)
	1-3	69 (63-76)
	3-5	50 (36-69)
	>5	2 (18-46)
201-350	<1	129 (91-166)
	1-3	50 (25-74)
	3-5	47 (24-69)
	>	23 (2-44)
>350	<1	90 (37-144)
	1-3	50 (18-82)
	3-5	17 (-17-51)
	>5	21 (-12-54)

We use this data to estimate the average time to progress through our CD4 categories whilst on effective cART. For people with undetectable viral load:

- For CD4 count increases from 0 to 200 cells per μL, average increases of 76 (53-99) cells per μL can be expected during the first year and then 69 (63-76) cells per μL during the second and third years. Therefore, it can be expected to take 2.80 (2.33-3.58) years to progress through this category.
- For CD4 count increases from 200 to 350 cells per μL, we have a 150 CD4 count increase. In this interval, the CD4 count increases by 129 (91-166) cells per μL during the first year and then 50 (25-74) CD4 count during the second year. Therefore, it can be expected to take 1.42 (0.9-3.42) years to progress through this category.
- For CD4 count increases from 350 to 500 cells per μL, then we have a 150 CD4 count increase. In this interval, the CD4 count increases by 90 (37-144) cells per μL during the first year and then 50 (18-82) cells per μL during the second year. Therefore, it can be expected to take 2.20 (1.07-7.28) years to progress through this category.

EuroSIDA study [26] investigated that the HCV serostatus does not influence CD4 recovery among patients on ART. It was found that there was no difference in CD4 gain among HIV/HCV coinfected and HIV mono-infected patients after starting ART. Therefore we assume the same recovery rate for HIV/HCV coinfected patient as HIV mono-infected patient.

d

15.4/100 person years is the average rate of stopping one regime due to toxicity but the vast majority usually start another regime [27]. Very few people who commence ART stop altogether (expert opinion). Therefore, we take the absolute rate of completely stopping therapy to range from 1-5% per year as an experimental variable.

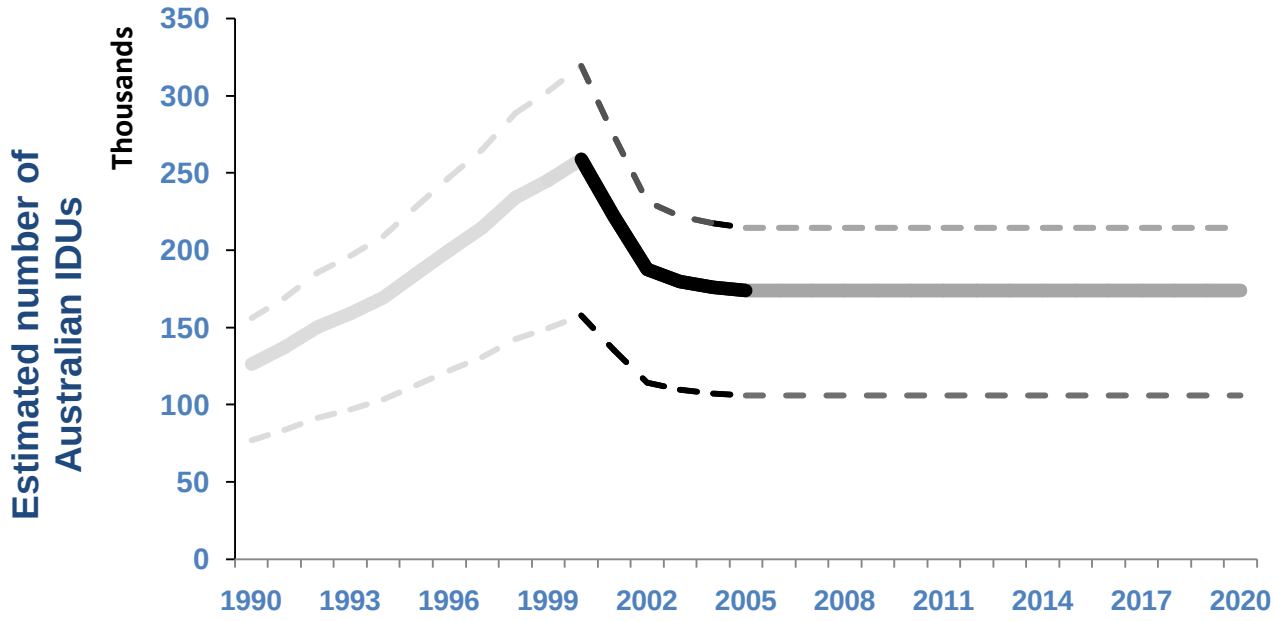
Table A.2: Parameters related to hepatitis C

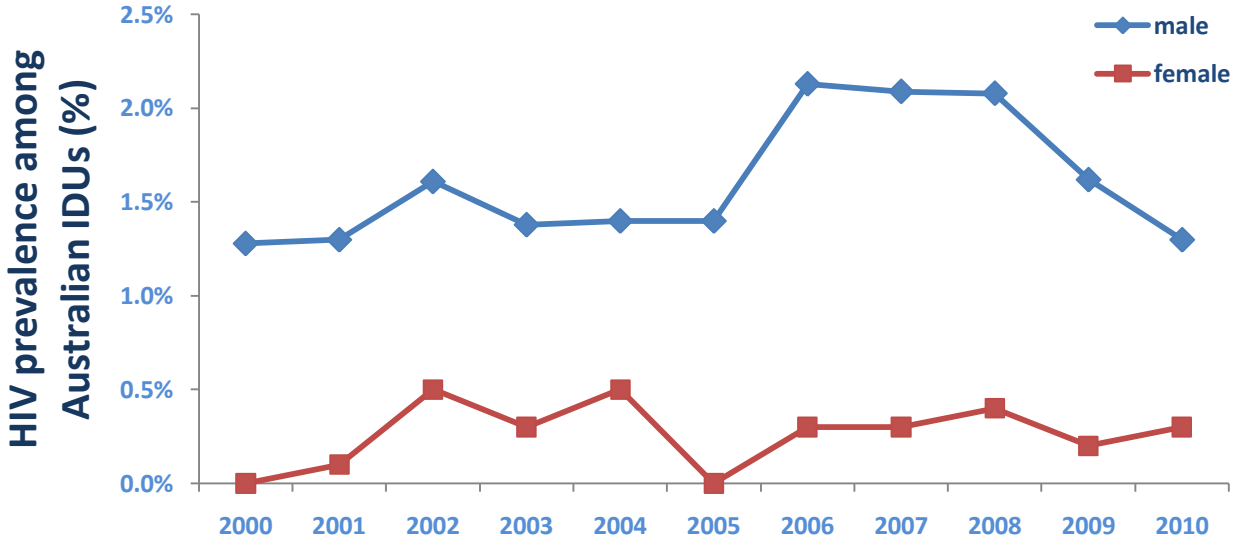
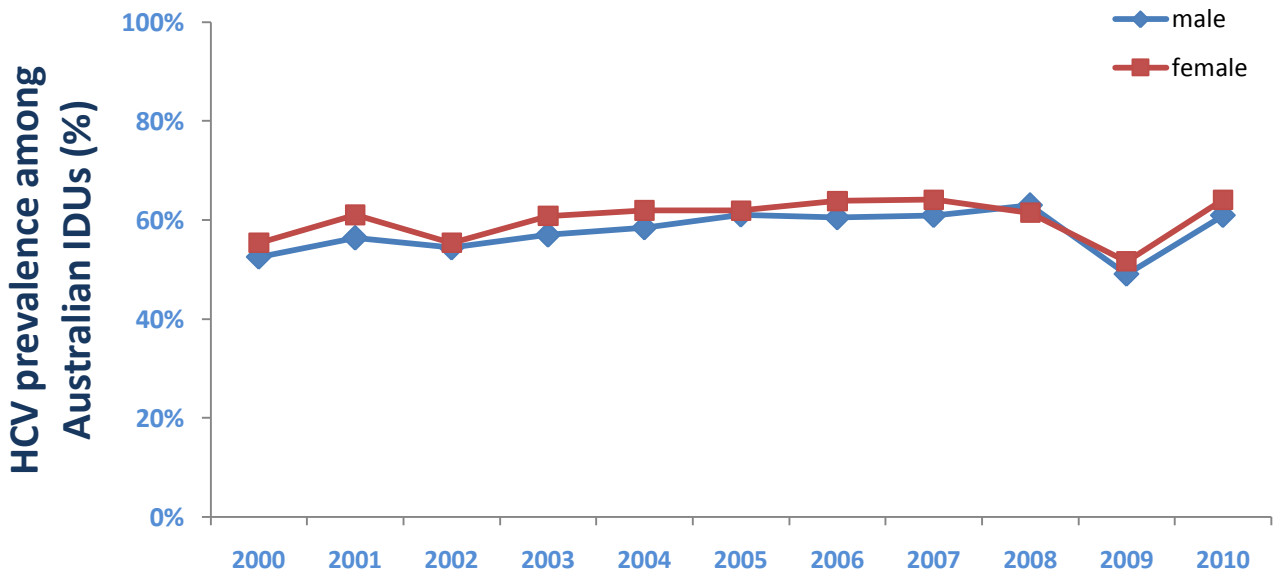
Symbol	Description		Values	References
Transmission				
β_{HCV}	Transmission probability of hepatitis C per injection with a contaminated syringe		1.5-4%	[23, 28-34], a
Testing Rate				
σ	Proportion of individuals to receiving HCV test every year		53-70%	[11]
Disease progression without treatment				
$1/\tau_A$	Average time for untreated HCV infected individuals to progress from **acute** infection to the first stage of fibrosis (**F0)**		4-8 months	[35, 36]
$1/\tau_{F0\_F1}$	Average time from fibrosis stage **F0** to **F1 [**Annual transition probability]		8.62 (0.23-16.95) years [0.116 (0.059-0.228)]	[37, 38]
$1/\tau_{F1\_F2}$	Average time from fibrosis stage **F1** to **F2** [Annual transition probability]		11.76 (9.09-15.38) years [0.085 (0.065-0.110)]	[37, 38]
$1/\tau_{F2\_F3}$	Average time from fibrosis stage **F2** to **F3** [Annual transition probability]		11.76 (6.80-20.41) years [0.085 (0.049-0.147)]	[37, 38]
$1/\tau_{F3\_F4}$	Average time from fibrosis stage **F3** to **F4** [Annual transition probability]		7.69 (3.13-18.87) years [0.130 (0.053-0.319)]	[37, 38]
$1/\tau_{F4\_LF}$	Average time from **F4** to **liver failure** [Annual transition probability]		18.18 (10.87-25.0) years [0.055 (0.040-0.092)]	[39-55], b
$1/\tau_{F4\_HCC}$	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)]	[55, 56]
$1/\tau_{LF\_LT}$	Average time from **liver failure** until **liver transplant** [Annual transition probability]		30.30 (20.41-58.82) years [0.033 (0.017-0.049)]	[57]
$1/\tau_{HCC\_LF}$	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)]	[58], c
$1/\mu_{LF}$	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)]	[44]
$1/\mu_{LT}$	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)]	[59, 60], d
		After first year	29.41 (23.26-41.67) years [0.034 (0.024-0.043)]	
$1/\mu_{HCC}$	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)]	[48]
Commencement of treatment				
$\frac{1}{\eta_A}$	Average time before individuals in **Acute/Early** HCV infection commence treatment	Asymptomatic	320 (213-399) days	e
		Symptomatic	221 (188-274) days	
η_F	Distribution of individuals commencing HCV treatment per year according to stage of fibrosis	F0/1	25-30%	[61]
		F2/3	46-60%	
		F4	15-25%	
Stopping treatment				

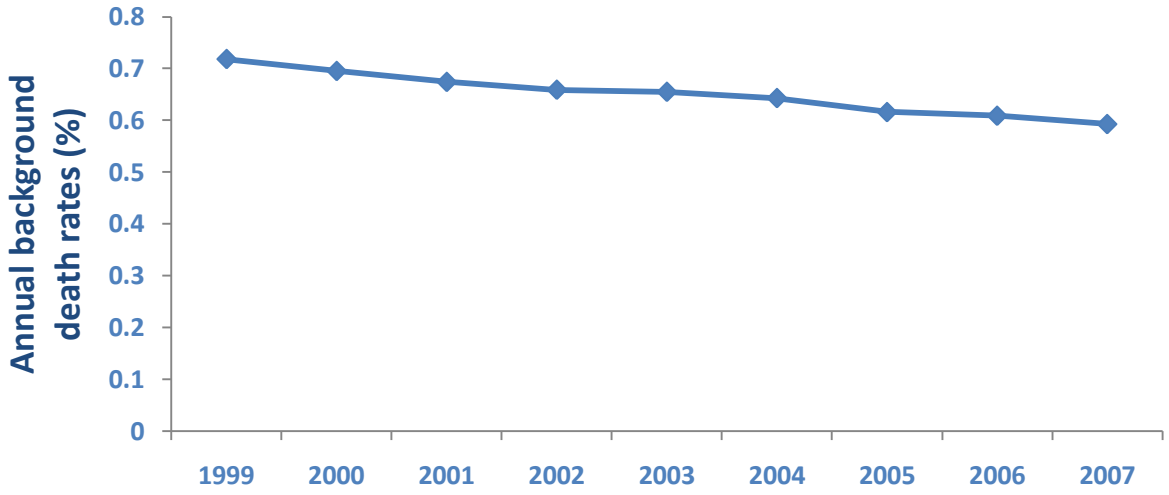
$\frac{1}{\nu}$	Average duration of treatment	Acute	0.46 years	[62]
		F0-F4	0.69 years	[63, 64]
Clearance of virus				
ψ	Proportion of IDUs who spontaneously clear HCV	Acute	0.26 (0.22-0.29)	[65]
γ_A	Proportion of HCV-treated individuals who clear the virus due to treatment (sustained virological responders) in **Acute** HCV		0.6-0.9	[66-70]
γ_{F0}	Proportion of HCV-treated individuals who clear the virus due to treatment in **F0** phase		0.60 (0.52-0.68)	[64, 71, 72]
γ_F	Proportion of HCV-treated individuals who clear the virus due to treatment in **F1-F4** phase		0.56 (0.50-0.61)	[63, 64, 71-77]
a	No study has directly estimated the probability of HCV transmission per injection by IDUs using a contaminated syringe. Numerous studies have estimated the transmission risk of HCV in an occupational setting due to needlestick injury [23, 28-34]. In the absence of other data, we use these studies to estimate transmission risk among IDUs sharing syringes. We reviewed these studies, paying particular attention on long-term cohort studies with larger number of cases, leading to a plausible range of transmission risk per exposure of 1.5-4%.			
b	Pooled estimate from a survey of the literature [39-55]; weighted using sample size.			
c	11 of 111 new HCV-related HCC reported cases in 2007in Australia received a liver transplant [58]. This leads to a 95% confidence interval of 5-18%.			
d	Our deterministic ordinary differential equation model assumes exponential rates. We determined the best-fitting exponential function over 40 years, leading to an average transition probability of 0.043 (0.0294, 0.0557) per year, which is equivalent to an average time of 23.26 (17.95-34.01).			
e	Based on unpublished data from the Australian Trial in Acute Hepatitis C (ATAHC) study.			

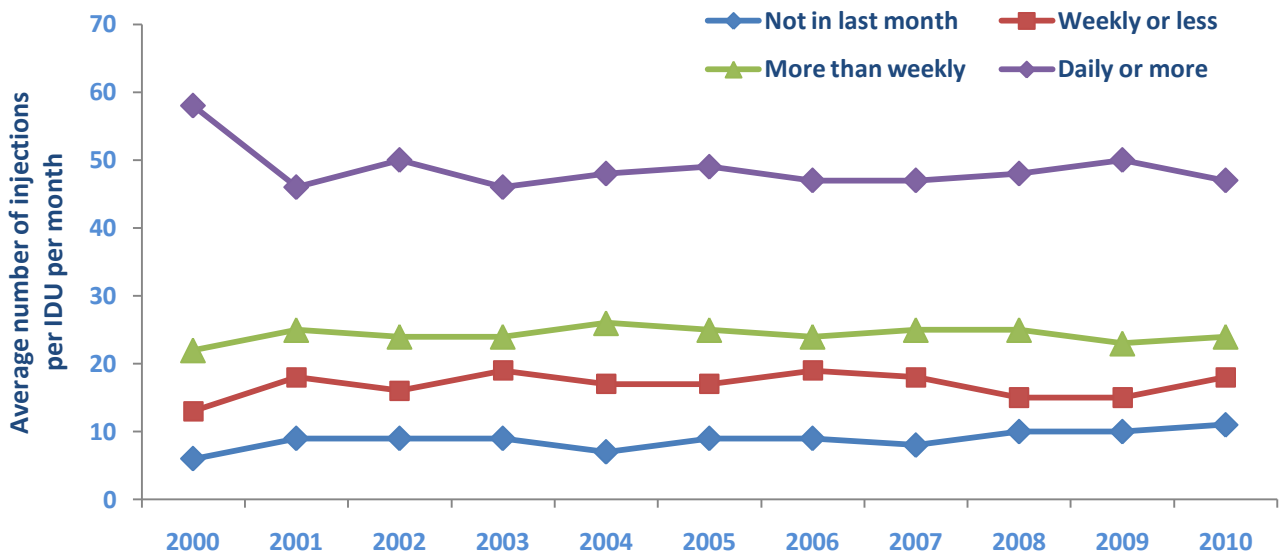
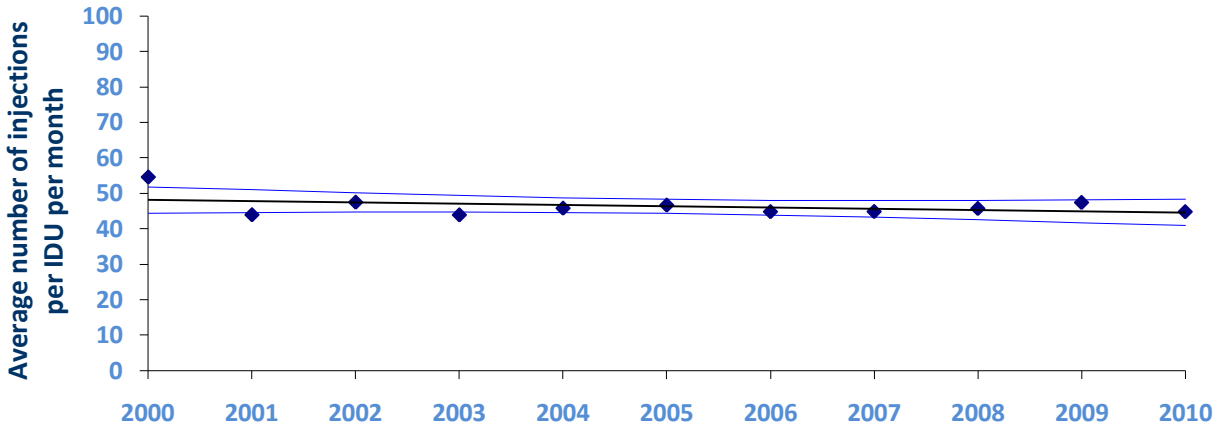
Table A.3: Demographic, epidemiological and behavioral parameters

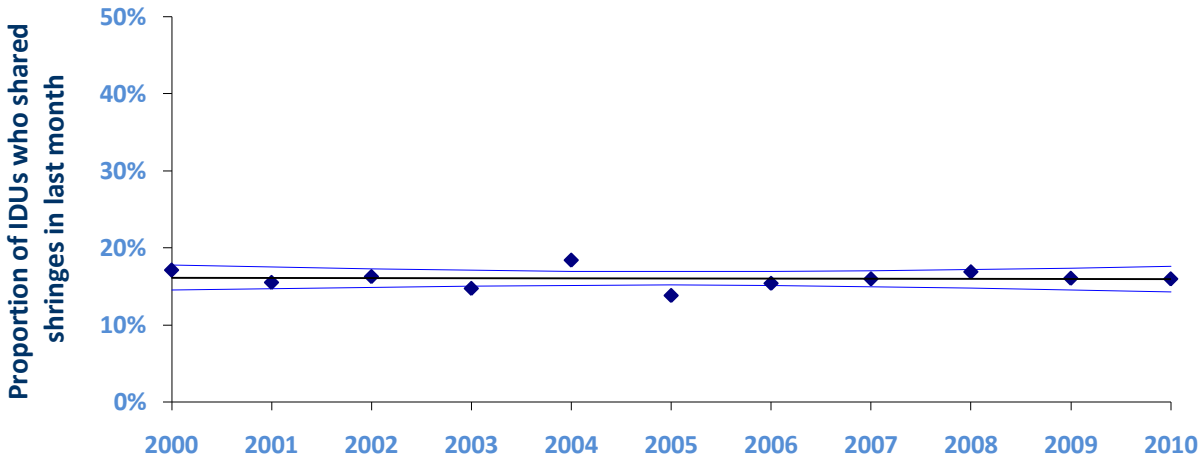
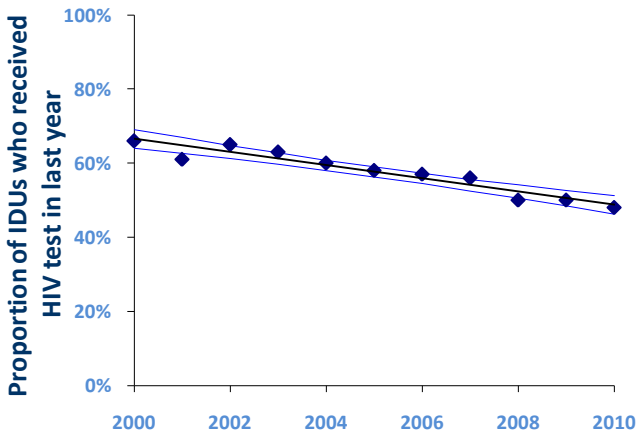
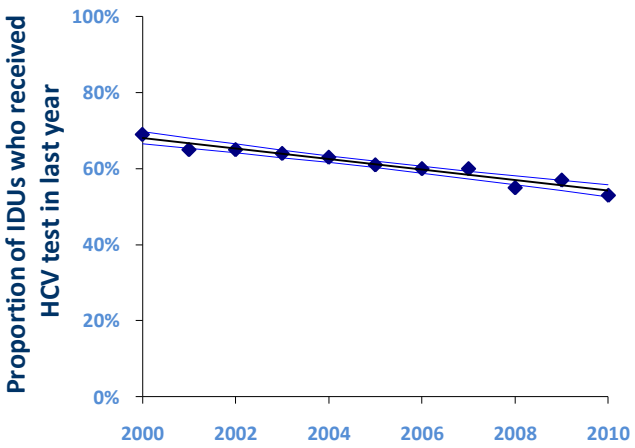
Symbol	Description	Values	References
N	Population size of IDUs	173,500 (105,000-236,500)	[11, 78], a
P	Total number of syringes distributed per year		b
Epidemiology parameters			
p_0^{HIV}	Prevalence of HIV among IDUs	1.17% (0.90- 1.40%)	c
p_0^{HCV}	Prevalence of HCV among IDUs		d
π	Average rate of people entering IDU population		e
μ	Annual background death rate (not drug-related or disease-related)	0.5-0.7%	f
ω	Percentage of syringes distributed that are not used	0.5-1%	Experimental variable
Behavioural parameters			
n	Average number of injections per IDU per year (weighted average over all injecting frequency stratifications)		g
s	Proportion of IDUs who share syringes		h
q	Proportion of injections that are shared for IDUs that share syringes	13-17%	[11]
η_{HIV}	Proportion of IDUs who received HIV test in last year		i
η_{HCV}	Proportion of IDUs who received HCV test in last year		i
Syringe cleaning parameters			
$p_c^{syringe}$	Proportion of syringes used by multiple people that are cleaned before re-use	5-10%	Experimental variable
p_c^{other}	Proportion of times other equipment (spoons, tourniquets, etc) that is used by multiple people is cleaned before re-use	1-5%	Experimental variable
$\varepsilon_c^{syringe}$	Effectiveness of syringe cleaning — HIV	60-75%	[79-81]

		HCV	25-35%	[82-86]
ε_c^{other}	Effectiveness of cleaning other equipment (spoons, tourniquets, etc)	HIV	70-80%	Experimental variable
		HCV	50-70%	
a	Using the same form for the change in the number of IDUs in Australia as that estimated by Law et al. [87], and adjusting slightly to the magnitude recently estimated by Mathers et al. [78], we assume that the IDU population in Australia has changed as shown below (the dashed regions refer to lower and upper bounds of confidence): 			
b	The total number of syringes distributed each year in Australia is shown in Figure 1 of the main manuscript.			

c	Below is a summary of HIV prevalence estimates among IDUs according to NSP survey data [11]. These data are consistent with sentinel and non-sentinel site data. Because of the low number of HIV cases detected, there is considerable variation. 
d	Below is a summary of HCV prevalence estimates among IDUs according to NSP survey data [11]. These data are consistent with sentinel and non-sentinel site data. 
e	The rate of entry of new IDUs into the population is determined dynamically based on the mortality rates to ensure that the total population size matches the assumed size (see footnote *a*).

f	From the Australian Demographic Statistic report [88, 89], the standardised annual death rates among Australians over time is shown below:  The annual background death rate is around 0.6-0.7%. From the D:A:D study [15], the CVD, liver disease, renal or non-AIDS related death rate was estimated to be 0.5 (0.488-0.59%) per year. The Illicit drug use expert group conducted a systematic review of mortality rates among IDUs [90] and reported that Australia had the lowest mortality rate of any world region, where data were available, and their mortality rate estimate was 0.86% (0.83-0.89%) per year [90]. The Victorian Injecting cohort Study (VICS) estimated the overall annual mortality rate among IDUs as 0.83% (0.56-1.21%) [91]. This includes drug overdose mortality and additional drug-related mortality rates. Therefore, a range of 0.86% (0.56-1.21%) per year, to cover all possible uncertainty. Several longitudinal studies also estimated the rates of mortality of patients who commence opioid maintenance treatment [92, 93]. The overall mortality rate among those patients were 0.88% among patients who receive the treatment with drug-overdose mortality rate of 0.35% and AIDS-related mortality rate of 0.059%. Therefore, we assume 0.5-0.7% for an annual background death rate.

g	From the NSP survey data [11], the proportions of IDUs who did not inject in the last month, injected weekly or less, injected more than weekly, injected once daily or more were estimated over time as shown below:  We assume that IDUs who did not inject in the last month inject an *average* of once every 2 months, those who inject weekly or less inject an *average* of once every fortnight, those that inject more than weekly inject once every 5 days on *average* and those who inject more than daily injected 1-5 time. Mean and 95% confidence intervals for the trend in injecting frequency was calculated as follows: 

h	Sharing rates among Australian IDUs were obtained from the Australian NSP Survey [11]. Regression analysis determined the mean and 95% confidence intervals for the trend in sharing rates over time: 
i	Testing rates for HIV and HCV among Australian IDUs were obtained from the Australian NSP Survey [11]. Regression analysis determined the mean and 95% confidence intervals for the trend in testing rates over time:  

Healthcare costs and health utilities

Table A.4: Healthcare costs (annual cost per person in 2010 Australian dollars)

Healthcare costs for HIV	**Costs**	**Reference***
PLHIV who have CD4 count >500 cells per µl	$1,679	[94-97]
PLHIV who have CD4 count 350-500 cells per µl	$2,265	
PLHIV who have CD4 count 200-350 cells per µl	$3,010	
PLHIV who have CD4 count <200 cells per µl	$6,062	
Cost of first-line ART	$16,105	
Cost of second-line ART	$16,728	
Cost of subsequent lilnes of ART	$30,613	
Non-ART healthcare costs	$3,010	
Healthcare costs for HCV	**Costs**	**Reference***
Acute hepatitis C	$879	[94-97]
Pre-cirrhosis stage of chronic hepatitis C (fibrosis stage 0 to 3) – 1st year	$879	
Pre-cirrhosis stage of chronic hepatitis C (fibrosis stage 0 to 3) – successive years	$317	
Compensated cirrhosis (fibrosis stage 4)	$911	
Acute hepatitis C treatment	$11,883	
Treatment of chronic HCV patients with pegylated interferon and ribavirin (24 weeks)	$11,935	
Treatment of chronic HCV patients with pegylated interferon and ribavirin (48 weeks)	$20,758	
Hepatocellular carcinoma	$18,772	
Liver transplant (1st year)	$126,095	
Liver transplant (subsequent years)	$14,067	
Decompensated cirrhosis (liver failure)	$14,067	

* Outpatient items were valued from the Medicare Benefits Schedule[94] and Pharmaceutical Benefits Schedule[95]. The unit costs of admission were estimated by searching health department data on the frequency and proportions of admission to hospital with different health states of HCV and HIV[96] and then deriving a weighted average cost per admission in a health state using cost weights for admission to an Australian public hospital[97]. Client costs for the purchase of injection equipment were estimated from data on the number of sterile injection equipment provided through pharmacies and average client out-of-pocket cost of packs of sterile injection equipment.. All costs were estimated in 2008 Australian dollars and inflated to 2010 Australian dollars using the health consumer price index[98] .

Table A.5: Health state utilities

HIV	**Low estimates**	**Upper estimates**	**Reference**
Health utility of uninfected IDUs	0.64	0.85	[99-104]
Relative health utility of PLHIV with CD4 > 500	0.84	0.95	[105, 106]
Relative health utility of PLHIV with CD4 is 350-500	0.84	0.93	[105, 106]
Relative health utility of PLHIV with CD4 is 200-350	0.72	0.93	[105, 106]
Relative health utility of PLHIV with CD4 < 200	0.60	0.85	[105, 106]
Relative health utility of PLHIV on ART	0.70	0.90	[106-109]
HCV	**Low estimates**	**Upper estimates**	**Reference**
Relative health utility of PLHCV at acute stage	0.64	0.89	[100, 110, 111]
Relative health utility of PLHCV at F0 to F3 stage	0.64	0.89	[100, 110, 111]
Relative health utility of PLHCV at F4 stage	0.62	0.88	[100, 110, 111]
Relative health utility of PLHCV at liver failure stage	0.52	0.87	[100, 110, 111]

Relative health utility of PLHCV at HCC stage	0.54	0.80	[100, 111]
Relative health utility of PLHCV at liver transplant	0.64	0.89	[100, 111]

Model outcomes versus available data

Figure A.1: Calibrated HIV-related trajectories (median: solid curve, interquartile ranges: dashed curves) compared with available data (solid dots).

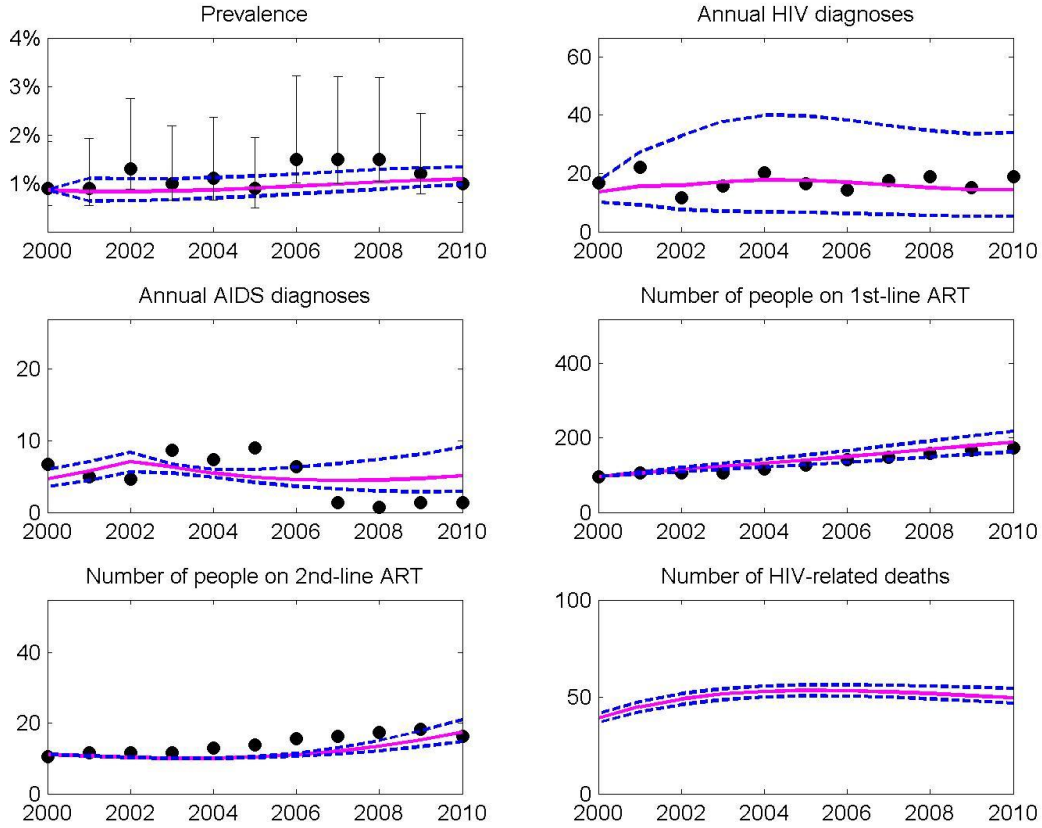
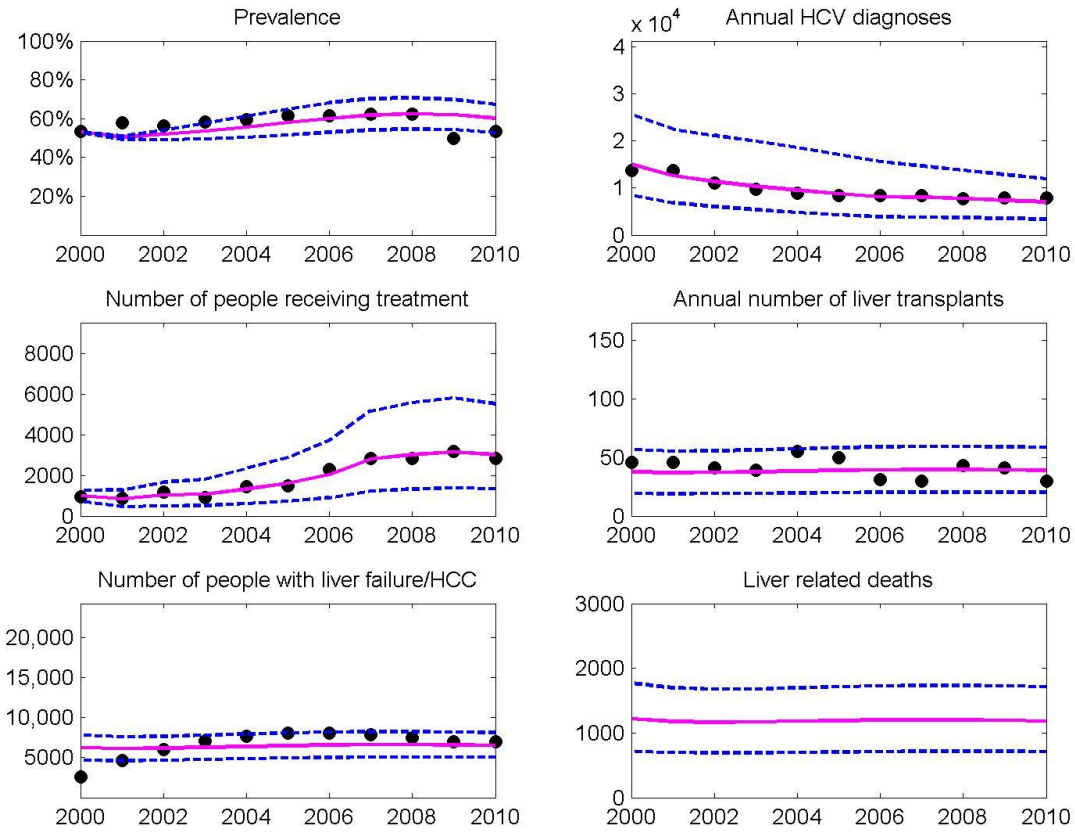


Figure A.2: Calibrated HCV-related trajectories (median: solid curve, interquartile ranges: dashed curves) compared with available data (solid dots).



Summary of economic results

Table A.6: Summary of economic results

Outcome (median, IQR)	Total QALYs	Gain in QALY (status quo – scenario)	Total healthcare costs	Cost savings (scenario-status quo)
Year 2000-2010*				
Current Status (status quo)	4,869,085		3,166m	
(5% adjusted)	(4,055,504-5,848,340)		(2,602-4,176)m	
Scenario 1: 25% sharing rate	4,847,455	13,596	3,238m	61m
(5% adjusted)	(4,029,282-5,838,940)	(8,646-16,736)	(2,661-4,238)m	(33-50)m
Scenario 2: 50% sharing rate	4,797,530	55,246	3,392m	228m
(5% adjusted)	(3,992,403-5,809,532)	(37,042-78,899)	(2,764-4,489)m	(168 311)m
Year 2000-Lifetime*				
Current Status (status quo)	10,128,497		5,003m	
(5% discounted)	(8,385,198-12,353,537)		(4,219-6,437)m	
Scenario 1: 25% sharing rate	10,092,139	26,505	5,266m	221m
(5% discounted)	(8,345,917-12,321,560)	(15,718-36,401)	(4,444-6,650)m	(166-248)m
Scenario 2: 50% sharing rate	10,043,383	99,369	5,762m	766m
(5% discounted)	(8,290,704-12,204,571)	(68,529-127,558)	(4,799-7,355)m	(646-861)m
Total NSP costs (adjusted for CPI)		$245m		
Incremental cost-effectiveness ratio (ICER)**		**2000-2010**		**2000-Lifetime**
25% sharing	undiscounted	25,664 (16,635-40,976)		24,163 (15,016-44,373)
	5% discounted	22,528 (14,590-36,263)		17,584 (11,299-31,373)
50% sharing	undiscounted	5,407 (3,739-7,986)		2,199 (1,786-2,952)
	5% discounted	4,436 (3,106-6,616)		2,466 (1,921-3,576)

* Adjusted for CPI with 2010 Australian dollars and discounted 5%. Results from 3% discounting are presented in the main manuscript.

** Incremental cost-effectiveness ratio (ICER) = incremental Costs/ incremental QALYs
= (total costs of investment + total costs of status quo –total costs of scenario)/(total QALYs of scenario – total QALYs of status quo).

Results from sensitivity analyses

Figure A.3: Tornado plot of partial rank correlation coefficients for the HIV incidence in 2010 with all model input parameters

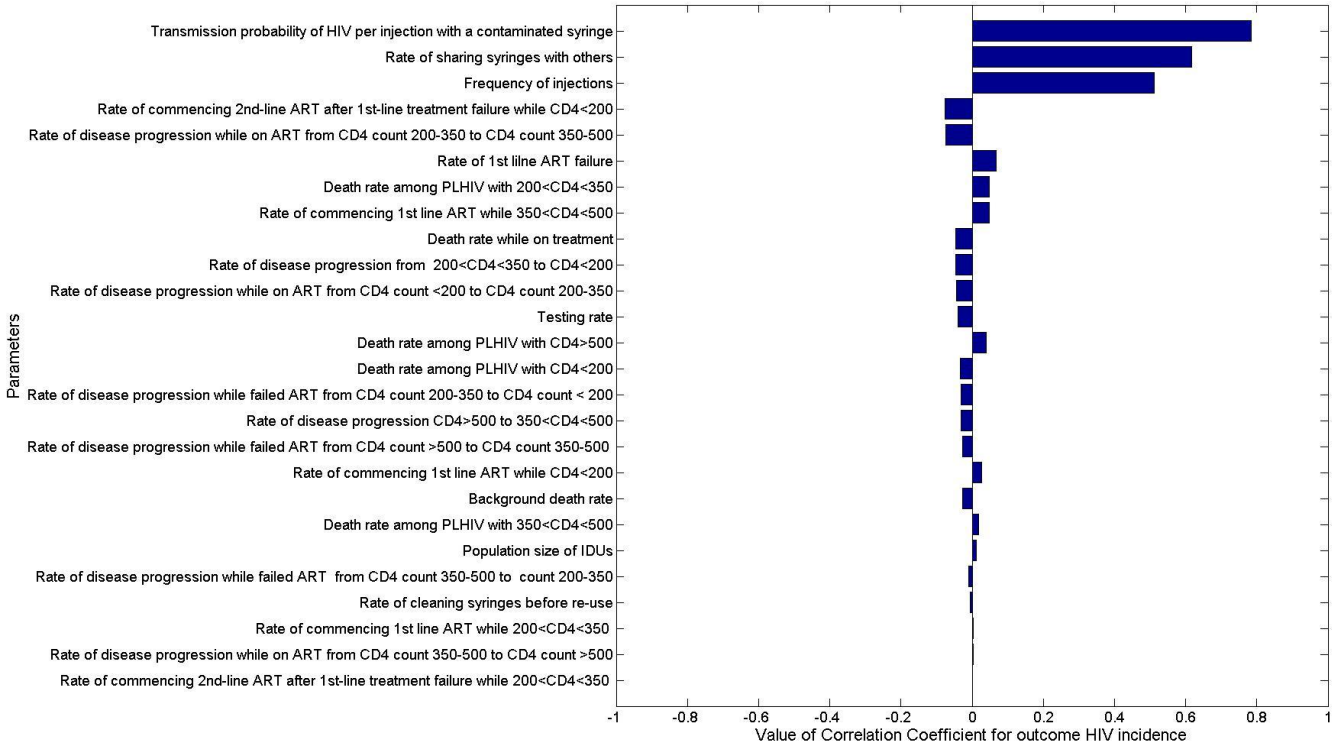
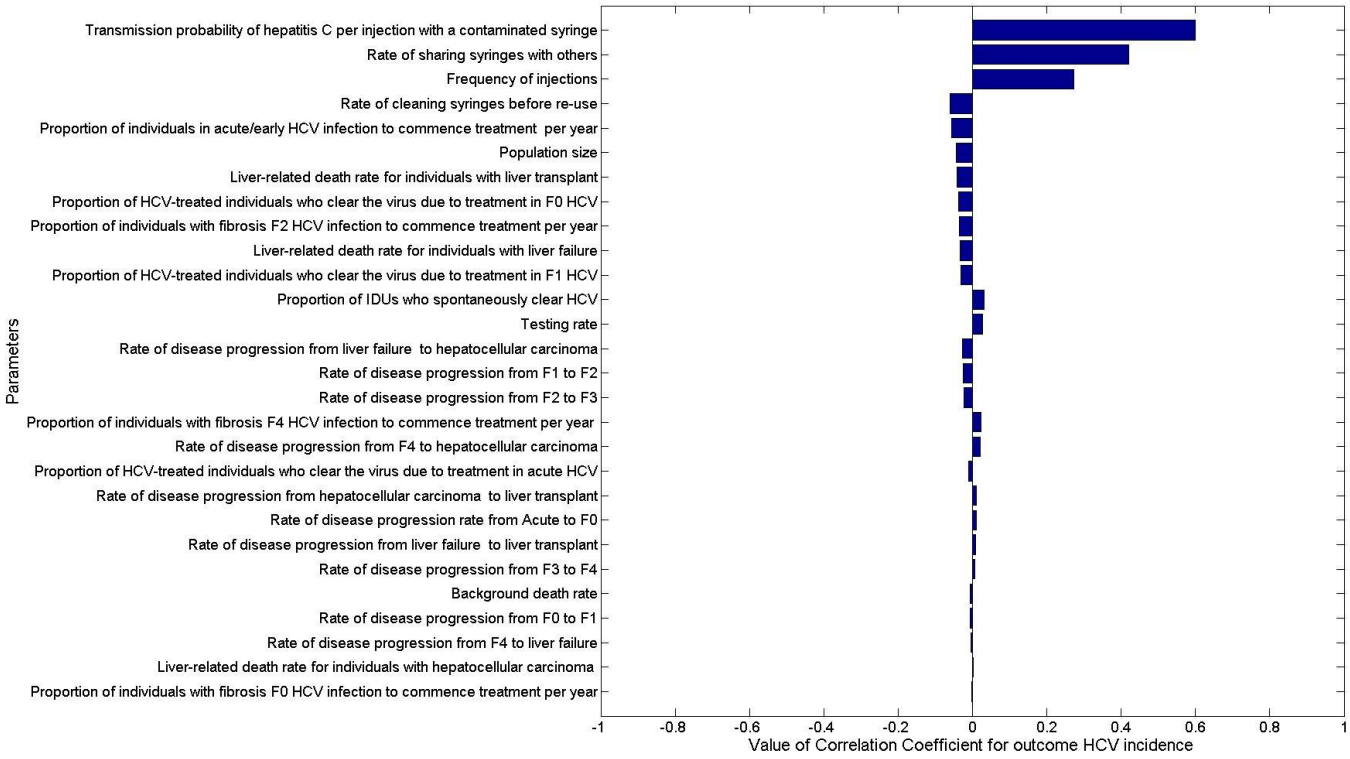


Figure A.4: Tornado plot of partial rank correlation coefficients for the HCV incidence in 2010 with all model input parameters



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