APPENDIX

Mathematical model

A dynamic, deterministic compartmental model of incarceration, injecting drug use, HCV transmission, progression, diagnosis, and treatment was adapted from a previously published model[1]. Schematics for the model components can be found in **appendix figures 1 and 2**. Susceptible PWID can become acutely infected with HCV by sharing injecting equipment with other infected PWID. We model a frequency dependent force of infection, such that an individual's risk of infection is proportional to the overall prevalence of infection. This model assumes a proportion (26%) of acutely infected PWID progress to chronic infection, with the remainder resolving their acute infection after a number of months and developing an antibody (Ab) response, thus becoming Ab+/RNA-. Those that develop chronic infection (Ab+/RNA+) remain infected and, unless diagnosed and successfully treated, progress through the various HCV disease stages (mild, moderate, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma (HCC), liver transplant, and post transplant). To incorporate HCV testing and subsequent treatment, we stratify the mild, moderate and compensated cirrhosis stages by diagnosis [undiagnosed, diagnosed but lost to follow-up and not in referral, diagnosed in early referral [1 year in community, 2 months in prison], and diagnosed and in late referral]. Ex-PWID who are uninfected are also stratified by whether they have been tested or not, hence those who have been tested would not be re-tested as they do not have a continuing infection risk. Death occurs from all stages, but elevated mortality rates were used from the decompensated cirrhosis, HCC, liver transplant, and post-transplant stages. If treated, infected PWID can achieve sustained viral response (SVR) whereby they are cured and if in the mild or moderate HCV stage are not at risk of progressing to a more advanced disease state, but remain at their current stage of liver progression and are susceptible to reinfection. For those who achieve SVR in the cirrhosis stage, we assumed a reduced rate of further liver disease progression compared to those who are still HCV infected, based on available data. These individuals are also susceptible to reinfection. If reinfected after achieving SVR, the PWID re-enters the infected compartment of their associated HCV disease stage. If a PWID fails treatment (non-SVR), they remain infected and can progress to more severe disease stages. Successfully treated

PWID can be reinfected and retreated, but those who do not achieve SVR are ineligible for retreatment. Due to reduced viral loads during treatment (even amongst those who relapse and do not achieve SVR), we assume PWID are not infectious during treatment[2, 3]. Current injectors are at risk of infection, but after permanent cessation of injecting do not have any infection risk. For simplicity, the model does not assume any behavioural heterogeneity among the PWID population (such as high/low risk), as modelling indicated introducing heterogeneity in risk does not have an undue influence on prevention intervention effectiveness as long as individuals circulate between high risk and intervention states[4].

In order to appropriately model incarceration, the model structure was replicated to track the flow of PWID and ex-PWID between never incarcerated, currently incarcerated, and formerly incarcerated states. In addition, compartments for never-PWID were added (never incarcerated, currently incarcerated, formerly incarcerated) to enable model calibration to general population incarceration data. This model structure was based on previously published mathematical models of PWID incarceration[5, 6], and it was assumed that incarceration and re-incarceration rates of ex-PWID were equal to that of never-PWID. The model assumes that prisoners only share with other prisoners. Similarly, outside prison, we did not assume any difference in sharing behaviour between those who are never imprisoned or previously imprisoned, and these individuals share between each other.

This model incorporates HCV testing in the community as well as prison. Therefore, we model movement in/out of prison for current/ex/never PWID. Additionally, for PWID not imprisoned (never imprisoned and formerly imprisoned) we further stratified movement by contact with addiction services (in contact/not in contact). We assumed only those in contact with addiction services could be tested in addiction services. We also assumed that on release from prison, PWID were not immediately in contact with addiction services. Finally, not in incarcerated, all PWID and ex-PWID can be tested/diagnosed in other settings (which includes general practice, emergency room, etc).

Finally, the model was split into 7 age compartments ([15-19],[20-24],[25-29],[30-54],[55-64],[65-74],[75+]), with individuals entering the model at age 15-19 as never-

PWID. In total, the model consists of 222 states and 7 age stratifications, leading to 222 x 7=1,554 compartments.

The dynamic transmission aspect of the model is similar to our previously published mathematical models. Let $P^{n}_{m,a,I}$ represent the number of PWID, where the superscript *m* represents incarceration status (*m*=0,1,2 for never, currently, formerly incarcerated, respectively), the superscript n represents addiction services status (*n*=*out* for out of contact and *n*=*in* in contact, and noting that n=*out* for all incarcerated states when *m*=1), subscript *a* represents the age group, with *a*=1,2…7 for each age group. The subscript *I* represents the HCV state, where $I=x_i$ for susceptible where *i* represents the different susceptible stages (never infected, spontaneously cleared), $I=y_i$ for chronic infected undiagnosed (including mild, moderate, compensated cirrhosis), $I=z_i$ for chronic infected diagnosed (including mild, moderate, compensated cirrhosis, decompensated cirrhosis, HCC, liver transplant, post-transplant and in early referral, late referral, or lost to follow-up states), $I=v_i$ for on treatment (including mild, moderate, compensated cirrhosis), $I=s_i$ for SVR (mild, moderate, compensated cirrhosis) and $I=f_i$ for treatment failure/non-SVR (mild, moderate, compensated cirrhosis). For example, $P^{out}_{0,1,z1}$ represents a PWID who has never been imprisoned and is not in contact with addiction services, is in age group 1 (15-19), and is undiagnosed mild chronically infected. We assume proportionate mixing by age. Using this notation, the force of infection for a PWID who is not imprisoned (*m*=0 or 2) is:

$$\pi \frac{\sum_{\text{all } a,n,y_i,z_i,f_i} (P^{n}_{0,a,y_i}+P^{n}_{0,a,z_i}+P^{n}_{0,a,f_i}+P^{n}_{2,a,y_i}+P^{n}_{2,a,z_i}+P^{n}_{2,a,f_i})}{\sum_{\text{all } a,n,x_i,y_i,z_i,v_i,s_i,f_i} (P^{n}_{0,a,x_i}+P^{n}_{0,a,y_i}+P^{n}_{0,a,z_i}+P^{n}_{0,a,v_i}+P^{n}_{0,a,s_i}+P^{n}_{0,a,f_i}+P^{n}_{2,a,x_i}+P^{n}_{2,a,y_i}+P^{n}_{2,a,z_i}+P^{n}_{2,a,v_i}+P^{n}_{0,a,s_i}+P^{n}_{2,a,f_i})}$$

where π represents the infection rate, which is fit to the HCV prevalence among PWID.

While incarcerated, PWID can only transmit to other incarcerated PWID, so the force of infection for a susceptible PWID in prison (*m*=1) is:

$$\pi \frac{\sum_{\text{all } a,y_i,z_i,f_i} (P_{1,a,y_i}+P_{1,a,z_i}+P_{1,a,f_i})}{\sum_{\text{all } a,x_i,y_i,z_i,v_i,s_i,f_i} (P_{1,a,x_i}+P_{1,a,y_i}+P_{1,a,z_i}+P_{1,a,v_i}+P_{1,a,s_i}+P_{1,a,f_i})}$$

As stated before, all PWID in never infected (Ab-/RNA-), spontaneously cleared (Ab+/RNA-), and SVR states are susceptible for infection as described above.

Model Parameters

Testing rates

We fitted an overall PWID annual testing rate to calibrate the model to the estimated proportion of PWID who are diagnosed (approximately 50%[7]). This rate varied for each sampled group of parameters, but the mean annual testing rate was 12% per year among undiagnosed PWID. This annual testing rate ensured the proportion of diagnosed PWID remained stable (at equilibrium) without any intervention.

From this overall testing rate, we estimate the setting specific baseline testing rates occurring in various settings (prison, addiction services, other settings) as described in detail in our previous publication[1]. Through this, we estimate the overall annual baseline testing rate in prisons at 8% of PWID entrants, or approximately 6% of all prison entrants per year, consistent with the testing rate reported from across the prison system prior to the introduction of opt-out testing (6% in 2013[8]).

Testing costs

Costs associated with testing were calculated as follows. The numbers of PWID tested in each setting were calculated, and associated with setting specific test costs. Two additional costs were added: RNA testing (for all Ab+ tests) and non-PWID testing. The number of non-PWID tested in order to test one PWID was calculated from the setting-specific test yield (proportion of tests Ab+) and ‘true’ baseline prevalence. A setting with a low yield indicates more non-PWID are tested for every PWID; if yield equals baseline prevalence, this indicates only PWID are tested.

Model fitting

We use the results of 1000 fitted parameter sets from our previous publication as model inputs for this model, with the exception that the model was refit to produce a total of 10000 prisoners (5,000,000 total individuals, based on our calibrated

prevalence of prisoners at 0.2% of the general population). A multi-step parameter sampling and model calibration/fitting method was used with simplified models to reduce computational time and allow for verification of full model predictions against the simplified models. The full details of the sampling and model calibration/fitting method can be found in the main text and supplementary information of our previous publication[1].

Incarceration calibration

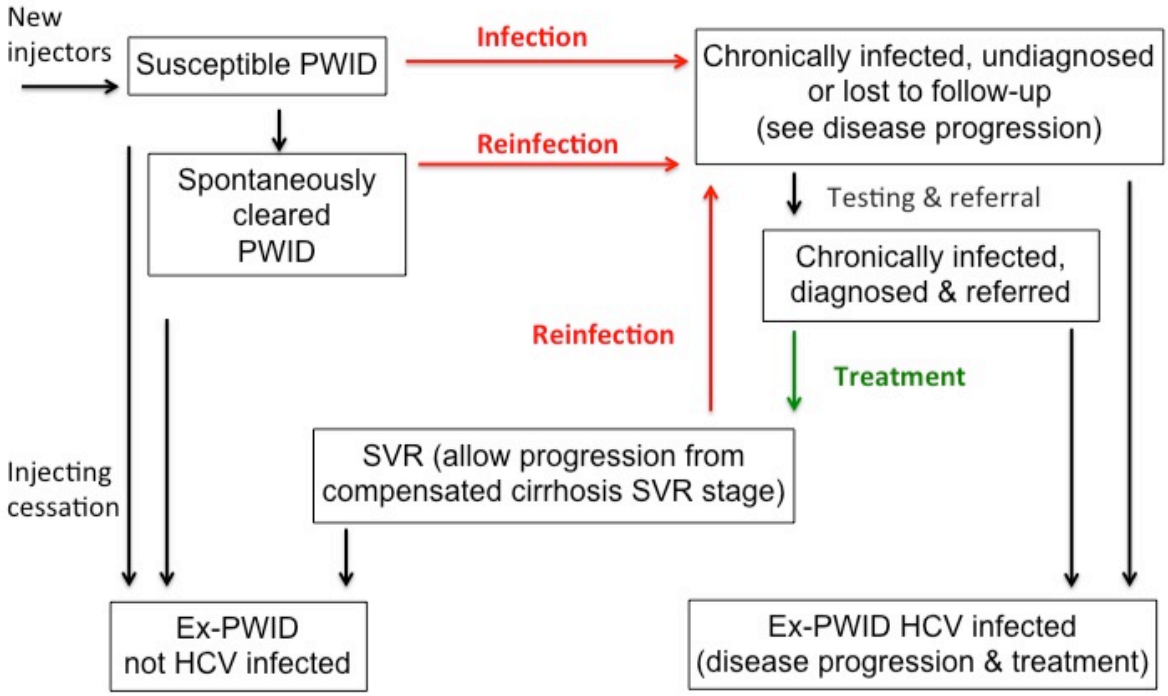
Briefly, to fit the incarceration dynamics, a simplified incarceration model (which neglected HCV transmission, testing, and treatment, see details in[1]) was run with inputs which included sampled parameters for cessation rate, overdose rate, and PWID prison release rate, and non-sampled input parameters estimated from literature/sources (age-specific death rates, prison release rates for never PWID, distribution of ages of first injection, and a preliminary estimate of the entry rate of never-PWID aged 15-19). The model was then calibrated to age-structured data on the proportion of the general population with a custodial sentence[9], proportion of PWIDs previously imprisoned, age distribution of current prisoners[10], proportion of prisoners ever PWID, proportion of the population currently imprisoned[11, 12], and the prevalence of PWID in the general population[13]. The parameters which were estimated through model calibration were the age-dependent incarceration rate, reincarceration rates, PWID incarceration rates, PWID reincarceration rates, and injecting initiation rate. The epidemiological and prison parameters sampled for this fitting algorithm can be found in **Table 1.** Model fitting was performed by using nonlinear least-squares methods using the MATLAB solver *lsqnonlin*.

Appendix figure 3 provides an example of the data and calibrated model projections with the median values chosen for each parameter; all other fits were similar to this. The model fitted well to the data, with the notable exception of the proportion of PWID previously incarcerated in the 15-19 age group, which the model consistently underestimates. This was due to the low proportion of prisoners who admit ever-injecting in this age group, along with the low general rates of ever incarceration in this age group. It was decided *a posteriori* that this deviation was acceptable given the goodness of fit to the rest of the data and also because it is unlikely that the data sources are consistent.

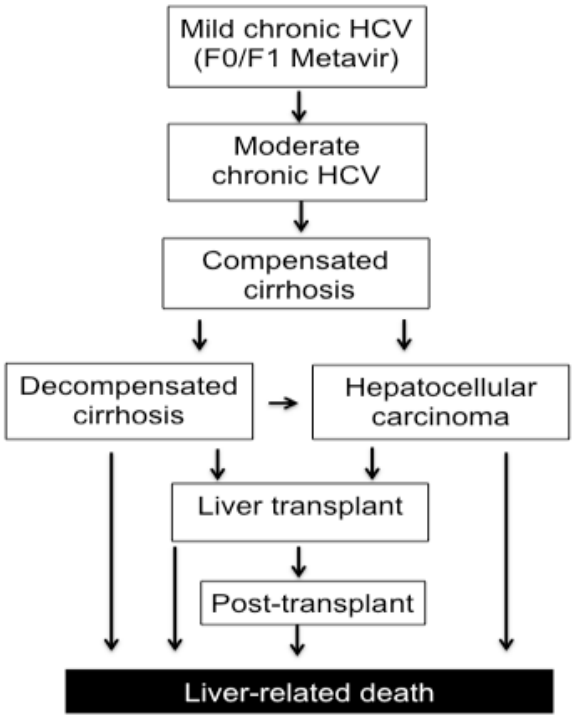
Initial conditions

The steady-state values of the full model without testing and treatment were used as initial conditions for the baseline/intervention simulations, with the following alterations. At the model start, the proportion of diagnosed ex-PWID was not thought to be at steady-state. This was because recent testing initiatives have mainly targeted PWID; it is estimated the proportion of diagnosed PWID (50%[7]) is currently likely higher than that of ex-PWID (estimated at 30% based on proportion PWID diagnosed in 2000 who are likely to be ex-PWID[14]). Hence, the steady-state values for infected populations were divided between undiagnosed/diagnosed states for the initial conditions based on these estimates. Due to very low treatment rates among PWID, we assume that no PWID have been treated prior to 2015. As it is unknown what proportion of previously diagnosed PWID are currently in referral for treatment, we assume that all previously-diagnosed are lost-to-follow-up at the beginning of the model, and hence need retesting in order to enter the referral and treatment pathway. For ex-PWID, we sample the proportion of ex-PWID previously treated (mean sampled value 10%[7]) from the range found in **table 1**. Of the remaining untreated proportion, 30% were considered diagnosed and were placed in the 'diagnosed and lost to follow-up' compartment. As a result of this initialisation procedure, the proportion of diagnosed ex-PWID was not at steady state at the start of the simulation. This was deemed appropriate, as recent testing initiatives have mainly targeted PWID, and therefore it is assumed that diagnosis rates among ex-PWID are low. However, over time those who are PWID will become ex-PWID, and therefore the proportion of diagnosed ex-PWID will increase over time.

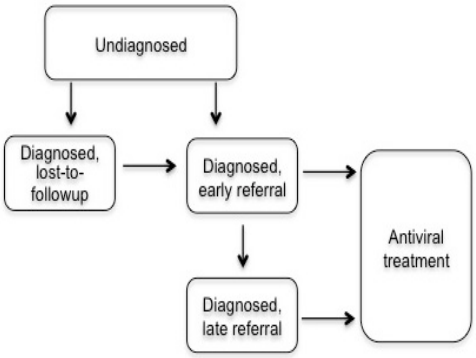
(a)


New injectors
Susceptible PWID
Infection
Chronically infected, undiagnosed or lost to follow-up (see disease progression)
Reinfection
Spontaneously cleared PWID
Testing & referral
Chronically infected, diagnosed & referred
Reinfection
Treatment
Injecting cessation
SVR (allow progression from compensated cirrhosis SVR stage)
Ex-PWID not HCV infected
Ex-PWID HCV infected (disease progression & treatment)

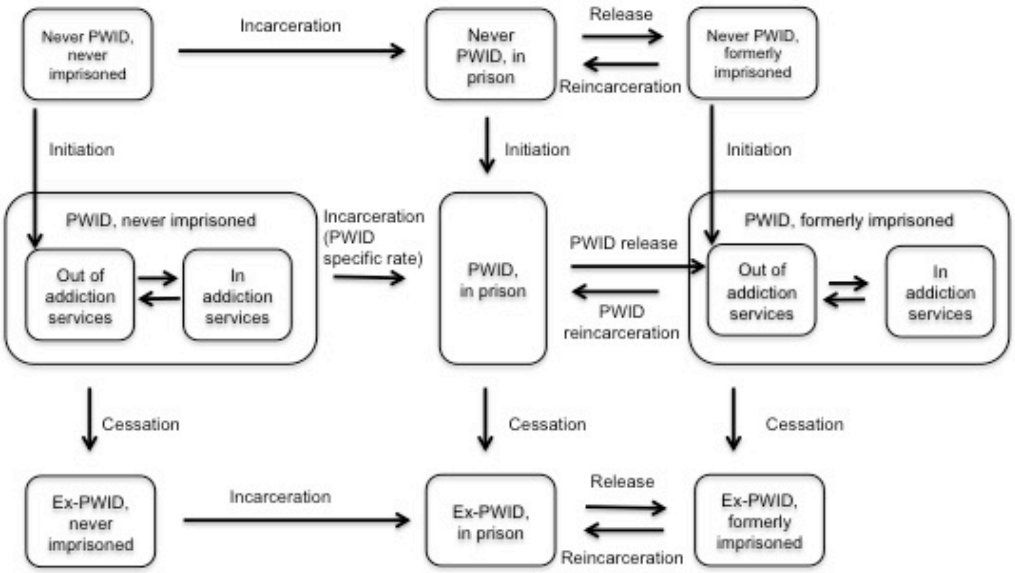
(b)


Mild chronic HCV (F0/F1 Metavir)
Moderate chronic HCV
Compensated cirrhosis
Decompensated cirrhosis
Hepatocellular carcinoma
Liver transplant
Post-transplant
Liver-related death

(c)

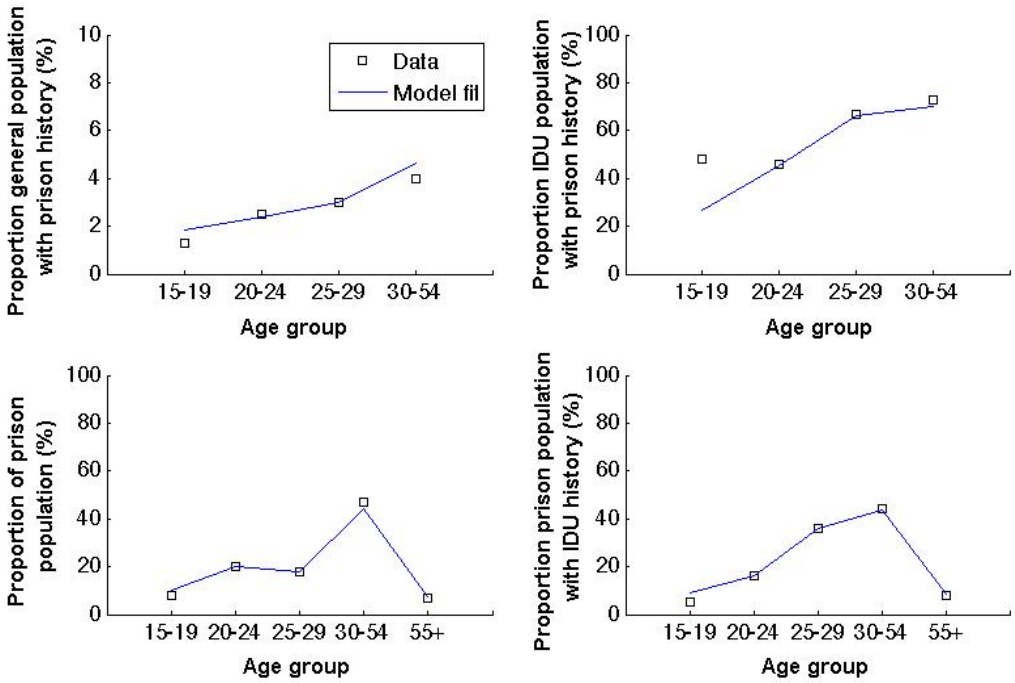


Appendix figure 1. HCV disease progression and diagnosis model schematics. Schematics show (a) HCV transmission among PWID, (b) HCV disease progression and (c) HCV diagnosis components. Note that we assume no disease progression for those who achieve SVR from the mild and moderate HCV stages; for those with compensated cirrhosis we assume a reduced rate of progression to later disease stages for those who achieve SVR. For those who are released from prison while in referral or treatment we assume no continuity of care, such that they are lost to follow-up on release and require re-testing in the community.



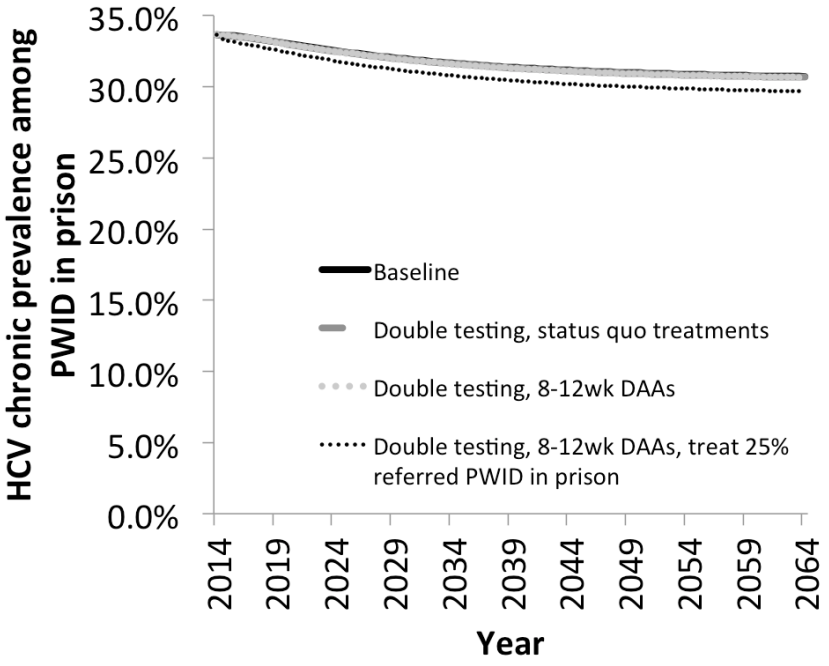
Model is stratified by age ([15-19, [20-24], [25-29], [30-54], [55-64], [65-74], [75+]), includes death from all compartments, overdose death from PWID compartments, and inflow to the youngest 'Never PWID, never imprisoned' compartment.

Appendix figure 2. General model flow schematic for incarceration and injecting drug use (each PWID and ex-PWID compartment includes HCV infection sub-compartments).

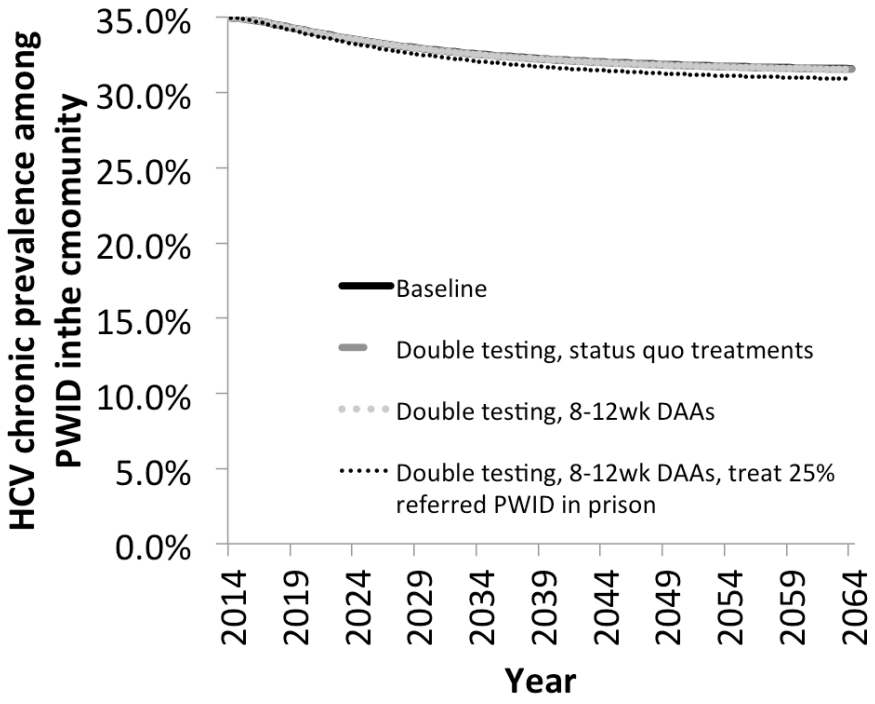


Appendix figure 3. Example of one characteristic model fit to the prison data (injecting duration 11 years, PWID incarceration duration 4 months, PWID overdose rate 1% per year). The top left shows the age-distributed proportion of general population with a custodial sentence. The bottom left shows the age-distribution within the prison population. The top right shows the proportion of PWID who have previously been incarcerated. The bottom right shows the proportion of prisoners who report ever PWID. Additionally, the model was fit to proportion of the general population imprisoned (simulated 0.21% as compared to 0.2%[11, 12]) and the proportion of population PWID (simulated 0.58% as compared to 0.65%[13])

(A)

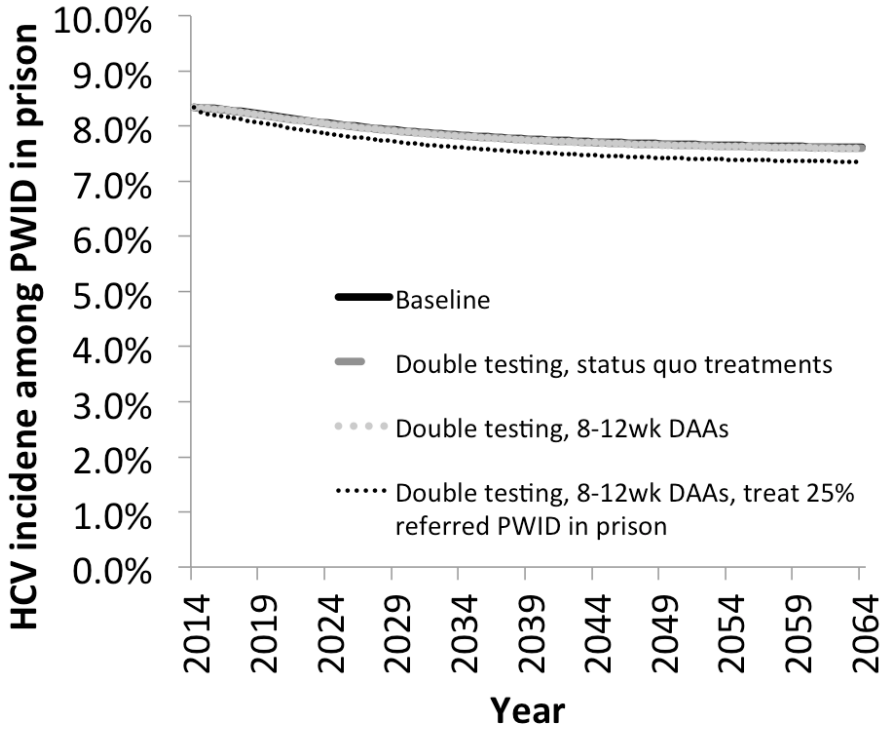


(B)

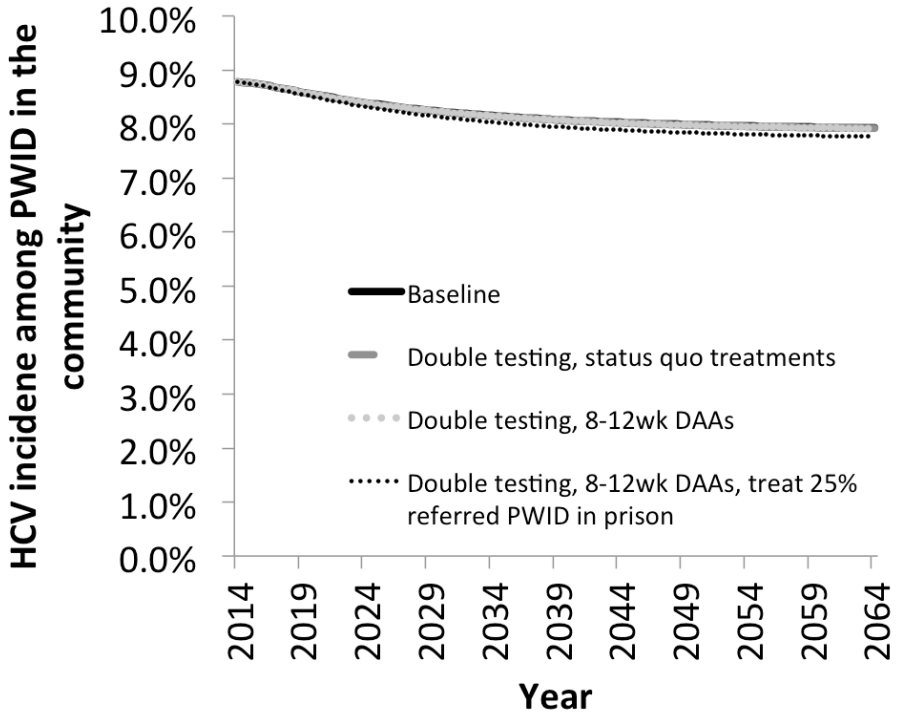


Appendix figure 3. HCV chronic prevalence over time among PWID in prison (A) and the community with various intervention scenarios. Median prevalence of 1,000 simulations shown.

(A)



(B)



Appendix figure 4. HCV incidence among PWID in prison (A) and the community (B) with various intervention scenarios. Median incidence of 1,000 simulations shown.

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