SUPPLEMENTARY MATERIAL

1. EQUATIONS FOR THE BASE-CASE ANALYSIS

The model includes compartments for uninfected PWID ($X_{j,k}$), chronically infected PWID ($C_{j,k}$), PWID on antiviral treatment ($T_{j,k}$), previously infected PWID ($E_{j,k}$), and PWID treatment failures ($F_{j,k}$). The population was stratified by intervention coverage: off/on HC_NSP (j=0 or 1, respectively), and off/on OST (k=0 or 1, respectively).

New PWID enter the model at a constant rate (θ) as uninfected, not on OST or HC_NSP. PWID can circulate through intervention coverage states; the per-capita recruitment rates onto OST and HC_NSP are β and η, respectively. PWID remain on OST and HC_NSP for durations of 1/γ and 1/κ, respectively.

All PWID are initially susceptible ($X_{j,k}$) and become HCV infected at a per-capita rate, force of infection $\lambda_{j,k}$, specific to that intervention state. The forces of infection for each susceptible state were defined by the relative risk in that state, such that infectivity and susceptibility were altered by a factor Γ, Π, or Β if the PWID was on OST, HC_NSP, or both, respectively. The chance of a PWID having a transmission event with any PWID from another risk state and infectious status was assumed to be proportional to the relative frequency of transmission events for PWID in that state. Due to the rapid reduction in viral loads while on antiviral treatment, we assume that the transmission potential of those on treatment is scaled down by a factor depending on the SVR rate.

A proportion (δ) spontaneously clear their acute infection and move to the previously infected compartment ($E_{j,k}$, characterized by HCV Ab+ and RNA- status) where they are at risk of reinfection. The remaining proportion (1-δ) proceed to the chronically infected compartment, $C_{j,k}$. PWID who are chronically infected can be put on antiviral treatment at a rate of Φ per 1000 PWID annually whereupon they enter the treatment compartment ($T_{j,k}$). If fewer than Φ per 1000 PWID are chronically infected (Φ>C), then Φ=C.

After a treatment with duration 1/ω, a proportion (α) attain sustained viral response (SVR) and move to the previously infected compartment, $E_{j,k}$, where they are at risk of reinfection. Those who do not attain SVR (1-α) move to the treatment failure compartment

where we assume they cannot be retreated due to a reluctance to undergo further therapy and potential resistance. PWID exit all compartments due to permanent cessation of drug use (μ_1) or death due to drug or non-drug related causes (μ_2).

The full model equations are as follows, for PWID not on HC_NSP and not on OST:

$$\frac{dX_{0,0}}{dt} = \theta - \lambda_{0,0}X_{0,0} + \kappa X_{1,0} + \gamma X_{0,1} - (\mu_1 + \mu_2 + \beta + \eta)X_{0,0}$$

$$\frac{dE_{0,0}}{dt} = \delta\lambda_{0,0}X_{0,0} - (1-\delta)\lambda_{0,0}E_{0,0} + \alpha\omega T_{0,0} + \kappa E_{1,0} + \gamma E_{0,1} - (\mu_1 + \mu_2 + \beta + \eta)E_{0,0}$$

$$\frac{dC_{0,0}}{dt} = (1-\delta)\lambda_{0,0}X_{0,0} + (1-\delta)\lambda_{0,0}E_{0,0} - f(C_{0,0}) + \kappa C_{1,0} + \gamma C_{0,1} - (\mu_1 + \mu_2 + \beta + \eta)C_{0,0}$$

$$\frac{dT_{0,0}}{dt} = f(C_{0,0}) - \omega T_{0,0} + \kappa T_{1,0} + \gamma T_{0,1} - (\mu_1 + \mu_2 + \beta + \eta)T_{0,0}$$

$$\frac{dF_{0,0}}{dt} = (1-\alpha)\omega T_{0,0} + \kappa F_{1,0} + \gamma F_{0,1} - (\mu_1 + \mu_2 + \beta + \eta)F_{0,0}$$

For PWID not on HC_NSP and on OST:

$$\frac{dX_{0,1}}{dt} = -\lambda_{0,1}X_{0,1} + \kappa X_{1,1} + \beta X_{0,0} - (\mu_1 + \mu_2 + \gamma + \eta)X_{0,1}$$

$$\frac{dE_{0,1}}{dt} = \delta\lambda_{0,1}X_{0,1} - (1-\delta)\lambda_{0,1}E_{0,1} + \alpha\omega T_{0,1} + \kappa E_{1,1} + \beta E_{0,0} - (\mu_1 + \mu_2 + \gamma + \eta)E_{0,1}$$

$$\frac{dC_{0,1}}{dt} = (1-\delta)\lambda_{0,1}X_{0,1} + (1-\delta)\lambda_{0,1}E_{0,1} - f(C_{0,1}) + \kappa C_{1,1} + \beta C_{0,0} - (\mu_1 + \mu_2 + \gamma + \eta)C_{0,1}$$

$$\frac{dT_{0,1}}{dt} = f(C_{0,1}) - \omega T_{0,1} + \kappa T_{1,1} + \beta T_{0,0} - (\mu_1 + \mu_2 + \gamma + \eta)T_{0,1}$$

$$\frac{dF_{0,1}}{dt} = (1-\alpha)\omega T_{0,1} + \kappa F_{1,1} + \beta F_{0,0} - (\mu_1 + \mu_2 + \square + \eta)F_{0,1}$$

For PWID on HC_NSP and not on OST:

$$\frac{dX_{1,0}}{dt} = -\lambda_{1,0}X_{1,0} + \eta X_{0,0} + \gamma X_{1,1} - (\mu_1 + \mu_2 + \beta + \kappa)$$

$$\frac{dE_{1,0}}{dt} = \delta\lambda_{1,0}X_{1,0}^{lo} - (1-\delta)\lambda_{1,0}^{lo}E_{1,0}^{lo} + \alpha\omega T_{1,0} + \eta E_{0,0} + \gamma E_{1,1} - (\mu_1 + \mu_2 + \beta + \kappa)E_{1,0}$$

$$\frac{dC_{1,0}}{dt} = (1-\delta)\lambda_{1,0}X_{1,0} + (1-\delta)\lambda_{1,0}E_{1,0} - f(C_{1,0}) + \eta C_{0,0} + \gamma C_{1,1} - (\mu_1 + \mu_2 + \beta + \kappa)C_{1,0}$$

$$\frac{dT_{1,0}}{dt} = f(C_{1,0}) - \omega T_{1,0} + \eta T_{0,0} + \gamma T_{1,1} - (\mu_1 + \mu_2 + \beta + \kappa)T_{1,0}$$

$$\frac{dF_{1,0}}{dt} = (1-\alpha)\omega T_{1,0} + \eta F_{0,0} + \gamma F_{1,1} - (\mu_1 + \mu_2 + \beta + \kappa)F_{1,0}$$

For PWID on HC_NSP and on OST:

$$\frac{dX_{1,1}}{dt} = -\lambda_{1,1}X_{1,1} + \eta X_{0,1} + \beta X_{1,0} - (\mu_1 + \mu_2 + \gamma + \kappa)X_{1,1}$$
$$\frac{dE_{1,1}}{dt} = \delta\lambda_{1,1}X_{1,1} - (1-\delta)\lambda_{1,1}E_{1,1} + \alpha\omega T_{1,1} + \eta E_{0,1} + \beta E_{1,0} - (\mu_1 + \mu_2 + \gamma + \kappa)E_{1,1}$$
$$\frac{dC_{1,1}}{dt} = (1-\delta)\lambda_{1,1}X_{1,1} + (1-\delta)\lambda_{1,1}E_{1,1} - f(C_{1,1}) + \eta C_{0,1} + \beta C_{1,0} - (\mu_1 + \mu_2 + \gamma + \kappa)C_{1,1}$$
$$\frac{dT_{1,1}}{dt} = f(C_{1,1}) - \omega T_{1,1} + \eta T_{0,1} + \beta T_{1,0} - (\mu_1 + \mu_2 + \gamma + \kappa)T_{1,1}$$
$$\frac{dF_{1,1}}{dt} = (1-\alpha)\omega T_{1,1} + \eta F_{0,1} + \square F_{1,0} - (\mu_1 + \mu_2 + \gamma + \kappa)F_{1,1}$$

With the force of infection:

$$\lambda_{0,0} = \pi \frac{(\Omega_{0,0} + \Gamma(\Omega_{0,1}) + \Pi(\Omega_{1,0}) + \mathrm{B}(\Omega_{1,1})}{\Omega_{0,0} + \Lambda_{0,0} + \Gamma(\Omega_{0,1} + \Lambda_{0,1}) + \Pi(\Omega_{1,0} + \Lambda_{1,0}) + \mathrm{B}(\Omega_{1,1} + \Lambda_{1,1})}$$
$$\lambda_{0,1} = \Gamma\lambda_{0,0}$$
$$\lambda_{1,0} = \Pi\lambda_{0,0}$$
$$\lambda_{1,1} = \mathrm{B}\lambda_{0,0}$$

where

$$\Omega_{j,k} = C_{j,k} + (1-\alpha)T_{j,k} + F_{j,k}$$

and

$$\Lambda_{j,k} = E_{j,k} + \alpha T_{j,k} + X_{j,k}.$$

Treatments are allocated proportionally to population size, such that if the annual number treated is Φ, then if all PWID are eligible for treatment,

$$f(C_{j,k}) = \begin{cases} \Phi \dfrac{C_{j,k}}{C_{0,0}+C_{0,1}+C_{1,0}+C_{1,1}}, & if\ \Phi \dfrac{C_{j,k}}{C_{0,0}+C_{0,1}+C_{1,0}+C_{1,1}} < C_{j,k} \\ C_{j,k}, & if\ \Phi \dfrac{C_{j,k}}{C_{0,0}+C_{0,1}+C_{1,0}+C_{1,1}} \geq C_{j,k} \end{cases}$$

and if PWID are only treated within OST, then

$$f(C_{j,1}) = \begin{cases} \Phi \dfrac{C_{j,1}}{C_{0,1}+C_{1,1}}, & if\ \Phi \dfrac{C_{j,1}}{C_{0,1}+C_{1,1}} < C_{j,1} \\ C_{j,k}, & if\ \Phi \dfrac{C_{j,1}}{C_{0,1}+C_{1,1}} \geq C_{j,1} \end{cases}$$

and

$$f(C_{j,0}) = 0.$$

2. EQUATIONS FOR THE SENSITIVITY ANALYSIS

In the sensitivity analysis, the model is further stratified by low and high risk PWID. For example, a PWID who has never been infected is $X_{j,k}^{risk}$, where we model high and low risk PWID populations (*risk*=*hi* or *lo*, respectively). For the main sensitivity analyses, PWID cannot circulate between high and low risk states (σ=0 and ζ=0), therefore the entry rate of new PWID is scaled such that the proportion high risk (ϕ) enter the high risk no intervention susceptible state, and the remainder (1-ϕ) enter the low risk no intervention susceptible state. If PWID circulate, then ϕ=σ/(σ+ζ), and the rates from low to high risk and from high to low risk are σ and ζ, respectively.

The full model equations are as follows, for low risk PWID not on HC_NSP and not on OST:

$$\frac{dX_{0,0}^{lo}}{dt} = \theta(1-\varphi) - \lambda_{0,0}^{lo}X_{0,0}^{lo} + \kappa X_{1,0}^{lo} + \gamma X_{0,1}^{lo} + \zeta X_{0,0}^{hi} - (\mu_1+\mu_2+\beta+\eta+\sigma)X_{0,0}^{lo}$$

$$\frac{dE_{0,0}^{lo}}{dt} = \delta\lambda_{0,0}^{lo}X_{0,0}^{lo} - (1-\delta)\lambda_{0,0}^{lo}E_{0,0}^{lo} + \alpha\omega T_{0,0}^{lo} + \kappa E_{1,0}^{lo} + \gamma E_{0,1}^{lo} + \zeta E_{0,0}^{hi} - (\mu_1 + \mu_2 + \square + \eta + \sigma)E_{0,0}^{lo}$$

$$\frac{dC_{0,0}^{lo}}{dt} = (1-\delta)\lambda_{0,0}^{lo}X_{0,0}^{lo} + (1-\delta)\lambda_{0,0}^{lo}E_{0,0}^{lo} - f(C_{0,0}^{lo}) + \kappa C_{1,0}^{lo} + \gamma C_{0,1}^{lo} + \zeta C_{0,0}^{hi} - (\mu_1 + \mu_2 + \beta + \eta + \sigma)C_{0,0}^{lo}$$

$$\frac{dT_{0,0}^{lo}}{dt} = f\left(C_{0,0}^{lo}\right) - \omega T_{0,0}^{lo} + \kappa T_{1,0}^{lo} + \gamma T_{0,1}^{lo} + \zeta T_{0,0}^{hi} - (\mu_1 + \mu_2 + \beta + \eta + \sigma)T_{0,0}^{lo}$$

$$\frac{\square F_{0,0}^{lo}}{dt} = (1-\alpha)\omega T_{0,0}^{lo} + \kappa F_{1,0}^{lo} + \gamma F_{0,1}^{lo} + \zeta F_{0,0}^{hi} - (\mu_1 + \mu_2 + \beta + \eta + \sigma)F_{0,0}^{lo}$$

For low risk PWID not on HC_NSP and on OST:

$$\frac{dX_{0,1}^{lo}}{dt} = -\lambda_{0,1}^{lo}X_{0,1}^{lo} + \kappa X_{1,1}^{lo} + \beta X_{0,0}^{lo} + \zeta X_{0,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \eta + \sigma)X_{0,1}^{lo}$$

$$\frac{dE_{0,1}^{lo}}{dt} = \delta\lambda_{0,1}^{lo}X_{0,1}^{lo} - (1-\delta)\lambda_{0,1}^{lo}E_{0,1}^{lo} + \alpha\omega T_{0,1}^{lo} + \kappa E_{1,1}^{lo} + \beta E_{0,0}^{lo} + \zeta E_{0,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \eta + \sigma)E_{0,1}^{lo}$$

$$\frac{dC_{0,1}^{lo}}{dt} = (1-\delta)\lambda_{0,1}^{lo}X_{0,1}^{lo} + (1-\delta)\lambda_{0,1}^{lo}E_{0,1}^{lo} - f(C_{0,1}^{lo}) + \kappa C_{1,1}^{lo} + \beta C_{0,0}^{lo} + \zeta C_{0,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \eta + \sigma)C_{0,1}^{lo}$$

$$\frac{dT_{0,1}^{lo}}{dt} = f\left(C_{0,1}^{lo}\right) - \omega T_{0,1}^{lo} + \kappa T_{1,1}^{lo} + \beta T_{0,0}^{lo} + \zeta T_{0,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \eta + \sigma)T_{0,1}^{lo}$$

$$\frac{dF_{0,1}^{lo}}{dt} = (1-\alpha)\omega T_{0,1}^{lo} + \kappa F_{1,1}^{lo} + \beta F_{0,0}^{lo} + \zeta F_{0,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \eta + \sigma)F_{0,1}^{lo}$$

For low risk PWID on HC_NSP and not on OST:

$$\frac{dX_{1,0}^{lo}}{dt} = -\lambda_{1,0}^{lo}X_{1,0}^{lo} + \eta X_{0,0}^{lo} + \gamma X_{1,1}^{lo} + \zeta X_{1,0}^{hi} - (\mu_1 + \mu_2 + \beta + \kappa + \sigma)X_{1,0}^{lo}$$

$$\frac{dE_{1,0}^{lo}}{dt} = \delta\lambda_{1,0}^{lo}X_{1,0}^{lo} - (1-\delta)\lambda_{1,0}^{lo}E_{1,0}^{lo} + \alpha\omega T_{1,0}^{lo} + \eta E_{0,0}^{lo} + \gamma E_{1,1}^{lo} + \zeta E_{1,0}^{hi} - (\mu_1 + \mu_2 + \beta + \kappa + \sigma)E_{1,0}^{lo}$$

$$\frac{dC_{1,0}^{lo}}{dt} = (1-\delta)\lambda_{1,0}^{lo}X_{1,0}^{lo} + (1-\delta)\lambda_{1,0}^{lo}E_{1,0}^{lo} - f(C_{1,0}^{lo}) + \eta C_{0,0}^{lo} + \gamma C_{1,1}^{lo} + \zeta C_{1,0}^{hi} - (\mu_1 + \mu_2 + \beta + \kappa + \sigma)C_{1,0}^{lo}$$

$$\frac{dT_{1,0}^{lo}}{dt} = f\left(C_{1,0}^{lo}\right) - \omega T_{1,0}^{lo} + \eta T_{0,0}^{lo} + \gamma T_{1,1}^{lo} + \zeta T_{1,0}^{hi} - (\mu_1 + \mu_2 + \beta + \kappa + \sigma)T_{1,0}^{lo}$$

$$\frac{dF_{1,0}^{lo}}{dt} = (1-\alpha)\omega T_{1,0}^{lo} + \eta F_{0,0}^{lo} + \gamma F_{1,1}^{lo} + \zeta F_{1,0}^{hi} - (\mu_1 + \mu_2 + \beta + \kappa + \sigma)F_{1,0}^{lo}$$

For low risk PWID on HC_NSP and on OST:

$$\frac{dX_{1,1}^{lo}}{dt} = -\lambda_{1,1}^{lo}X_{1,1}^{lo} + \eta X_{0,1}^{lo} + \beta X_{1,0}^{lo} + \zeta X_{1,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \kappa + \sigma)X_{1,1}^{lo}$$

$$\frac{dE_{1,1}^{lo}}{dt} = \delta\lambda_{1,1}^{lo}X_{1,1}^{lo} - (1-\delta)\lambda_{1,1}^{lo}E_{1,1}^{lo} + \alpha\omega T_{1,1}^{lo} + \eta E_{0,1}^{\square o} + \beta E_{1,0}^{lo} + \zeta E_{1,1}^{hi} - (\mu_1 + \mu_2 + \gamma + \kappa + \sigma)E_{1,1}^{lo}$$

$$\frac{dC_{1,1}^{lo}}{dt} = (1-\delta)\lambda_{1,1}^{lo}X_{1,1}^{lo} + (1-\delta)\lambda_{1,1}^{lo}E_{1,1}^{lo} - f(C_{1,1}^{lo}) + \eta C_{0,1}^{lo} + \beta C_{1,0}^{lo} + \zeta C_{1,1}^{hi} - (\mu_1+\mu_2+\gamma+\kappa+\sigma)C_{1,1}^{lo}$$
$$\frac{dT_{1,1}^{lo}}{dt} = f\left(C_{1,1}^{lo}\right) - \omega T_{1,1}^{lo} + \eta T_{0,1}^{lo} + \beta T_{1,0}^{lo} + \zeta T_{1,1}^{hi} - (\mu_1+\mu_2+\gamma+\kappa+\sigma)T_{1,1}^{lo}$$
$$\frac{dF_{1,1}^{lo}}{dt} = (1-\alpha)\omega T_{1,1}^{lo} + \eta F_{0,1}^{lo} + \beta F_{1,0}^{lo} + \zeta F_{1,1}^{hi} - (\mu_1+\mu_2+\gamma+\kappa+\sigma)F_{1,1}^{lo}$$

For high risk PWID not on HC_NSP and not on OST:

$$\frac{dX_{0,0}^{hi}}{dt} = \theta\varphi - \lambda_{0,0}^{hi}X_{0,0}^{hi} + \kappa X_{1,0}^{hi} + \gamma X_{0,1}^{hi} + \sigma X_{0,0}^{lo} - (\mu_1+\mu_2+\beta+\eta+\zeta)X_{0,0}^{hi}$$
$$\frac{dE_{0,0}^{hi}}{dt} = \delta\lambda_{0,0}^{hi}X_{0,0}^{hi} - (1-\delta)\lambda_{0,0}^{hi}E_{0,0}^{hi} + \alpha\omega T_{0,0}^{hi} + \kappa E_{1,0}^{hi} + \gamma E_{0,1}^{hi} + \sigma E_{0,0}^{lo} - (\mu_1+\mu_2+\beta+\eta+\zeta)E_{0,0}^{hi}$$
$$\frac{dC_{0,0}^{hi}}{dt} = (1-\delta)\lambda_{0,0}^{hi}X_{0,0}^{hi} + (1-\delta)\lambda_{0,0}^{hi}E_{0,0}^{hi} - f(C_{0,0}^{hi}) + \kappa C_{1,0}^{hi} + \gamma C_{0,1}^{hi} + \sigma C_{0,0}^{lo} - (\mu_1+\mu_2+\beta+\eta+\zeta)C_{0,0}^{hi}$$
$$\frac{dT_{0,0}^{hi}}{dt} = f\left(C_{0,0}^{hi}\right) - \omega T_{0,0}^{hi} + \kappa T_{1,0}^{hi} + \gamma T_{0,1}^{hi} + \sigma T_{0,0}^{lo} - (\mu_1+\mu_2+\beta+\eta+\zeta)T_{0,0}^{hi}$$
$$\frac{dF_{0,0}^{hi}}{dt} = (1-\alpha)\omega T_{0,0}^{hi} + \kappa F_{1,0}^{hi} + \gamma F_{0,1}^{hi} + \sigma F_{0,0}^{lo} - (\mu_1+\mu_2+\beta+\eta+\zeta)F_{0,0}^{hi}$$

For high risk PWID not on HC_NSP and on OST:

$$\frac{d\square_{0,1}^{hi}}{dt} = -\lambda_{0,1}^{hi}X_{0,1}^{hi} + \kappa X_{1,1}^{hi} + \beta X_{0,0}^{hi} + \sigma X_{0,1}^{lo} - (\mu_1+\mu_2+\gamma+\eta+\zeta)X_{0,1}^{hi}$$
$$\frac{dE_{0,1}^{hi}}{dt} = \delta\lambda_{0,1}^{hi}X_{0,1}^{hi} - (1-\delta)\lambda_{0,1}^{hi}E_{0,1}^{hi} + \alpha\omega T_{0,1}^{hi} + \kappa E_{1,1}^{hi} + \beta E_{0,0}^{hi} + \sigma E_{0,1}^{lo} - (\mu_1+\mu_2+\gamma+\eta+\zeta)E_{0,1}^{hi}$$
$$\frac{dC_{0,1}^{hi}}{dt} = (1-\delta)\lambda_{0,1}^{hi}X_{0,1}^{hi} + (1-\delta)\lambda_{0,1}^{hi}E_{0,1}^{hi} - f(C_{0,1}^{hi}) + \kappa C_{1,1}^{hi} + \beta C_{0,0}^{hi} + \sigma C_{0,1}^{lo} - (\mu_1+\mu_2+\gamma+\eta+\zeta)C_{0,1}^{hi}$$
$$\frac{dT_{0,1}^{hi}}{dt} = f\left(C_{0,1}^{hi}\right) - \omega T_{0,1}^{hi} + \kappa T_{1,1}^{hi} + \beta T_{0,0}^{hi} + \sigma T_{0,1}^{lo} - (\mu_1+\mu_2+\gamma+\eta+\zeta)T_{0,1}^{hi}$$
$$\frac{dF_{0,1}^{hi}}{dt} = (1-\alpha)\omega T_{0,1}^{hi} + \kappa F_{1,1}^{hi} + \beta F_{0,0}^{hi} + \sigma F_{0,1}^{lo} - (\mu_1+\mu_2+\gamma+\eta+\zeta)F_{0,1}^{hi}$$

For high risk PWID on HC_NSP and not on OST:

$$\frac{dX_{1,0}^{hi}}{dt} = -\lambda_{1,0}^{hi}X_{1,0}^{hi} + \eta X_{0,0}^{hi} + \gamma X_{1,1}^{hi} + \sigma X_{1,0}^{lo} - (\mu_1+\mu_2+\beta+\kappa+\zeta)X_{1,0}^{hi}$$
$$\frac{dA_{1,0}^{hi}}{dt} = \delta\lambda_{1,0}^{hi}X_{1,0}^{hi} - (1-\delta)\lambda_{1,0}^{hi}E_{1,0}^{hi} + \alpha\omega T_{1,0}^{hi} + \eta E_{0,0}^{hi} + \gamma E_{1,1}^{hi} + \sigma\square_{1,0}^{lo} - (\mu_1+\mu_2+\beta+\kappa+\zeta)E_{1,0}^{hi}$$
$$\frac{dC_{1,0}^{hi}}{dt} = (1-\delta)\lambda_{1,0}^{hi}X_{1,0}^{hi} + (1-\delta)\lambda_{1,0}^{hi}E_{1,0}^{hi} - f(C_{1,0}^{hi}) + \eta C_{0,0}^{hi} + \gamma C_{1,1}^{hi} + \sigma C_{1,0}^{lo} - (\mu_1+\mu_2+\beta+\kappa+\zeta)C_{1,0}^{hi}$$

$$\frac{dT_{1,0}^{hi}}{dt} = f\left(C_{1,0}^{hi}\right) - \omega T_{1,0}^{hi} + \eta T_{0,0}^{hi} + \gamma T_{1,1}^{hi} + \sigma T_{1,0}^{lo} - (\mu_1 + \mu_2 + \beta + \kappa + \zeta)T_{1,0}^{hi}$$
$$\frac{dF_{1,0}^{lo}}{dt} = (1-\alpha)\omega T_{1,0}^{hi} + \eta F_{0,0}^{hi} + \gamma F_{1,1}^{hi} + \sigma F_{1,0}^{lo} - (\mu_1 + \mu_2 + \beta + \kappa + \zeta)F_{1,0}^{hi}$$

For high risk PWID on HC_NSP and on OST:

$$\frac{dX_{1,1}^{hi}}{dt} = -\lambda_{1,1}^{hi}X_{1,1}^{hi} + \eta X_{0,1}^{hi} + \beta X_{1,0}^{hi} + \sigma X_{1,1}^{lo} - (\mu_1 + \mu_2 + \gamma + \kappa + \zeta)X_{1,1}^{hi}$$
$$\frac{dE_{1,1}^{hi}}{dt} = \delta\lambda_{1,1}^{hi}X_{1,1}^{hi} - (1-\delta)\lambda_{1,1}^{hi}E_{1,1}^{hi} + \alpha\omega T_{1,1}^{hi} + \eta E_{0,1}^{hi} + \beta E_{1,0}^{hi} + \sigma E_{1,1}^{lo} - (\mu_1 + \mu_2 + \gamma + \kappa + \zeta)E_{1,1}^{hi}$$
$$\frac{dC_{1,1}^{hi}}{dt} = (1-\delta)\lambda_{1,1}^{hi}X_{1,1}^{hi} + (1-\delta)\lambda_{1,1}^{hi}E_{1,1}^{hi} - f(C_{1,1}^{hi}) + \eta C_{0,1}^{hi} + \beta C_{1,0}^{hi} + \sigma C_{1,1}^{lo} - (\mu_1 + \mu_2 + \gamma + \kappa + \zeta)C_{1,1}^{hi}$$
$$\frac{dT_{1,1}^{hi}}{dt} = f\left(C_{1,1}^{hi}\right) - \square T_{1,1}^{hi} + \eta T_{0,1}^{hi} + \beta T_{1,0}^{hi} + \sigma T_{1,1}^{lo} - (\mu_1 + \mu_2 + \gamma + \kappa + \zeta)T_{1,1}^{hi}$$
$$\frac{dF_{1,1}^{hi}}{dt} = (1-\alpha)\omega T_{1,1}^{hi} + \eta F_{0,1}^{hi} + \beta F_{1,0}^{hi} + \sigma F_{1,1}^{lo} - (\mu_1 + \mu_2 + \gamma + \kappa + \zeta)F_{1,1}^{hi}$$

In this model, the forces of infection for each susceptible state were defined by the intervention coverage and risk status. The force of infection assumes that PWID either mix assortatively with probability 'ξ' or otherwise randomly (dependent on the relative number of possible HCV transmission events provided by each), with probability '1- ξ'. The force of infection for those in the high risk group is assumed to be a factor 'Ξ' greater than for those in the low risk group.

$$\lambda_{0,0}^{lo} = \pi(\xi\Psi_{lo} + (1-\xi)\Upsilon)$$
$$\lambda_{0,1}^{lo} = \Gamma\lambda_{0,0}^{lo}$$
$$\lambda_{1,0}^{lo} = \Pi\lambda_{0,0}^{lo}$$
$$\lambda_{1,1}^{lo} = \mathrm{B}\lambda_{0,0}^{lo}$$
$$\lambda_{0,0}^{hi} = \pi\Xi(\xi\Psi_{hi} + (1-\xi)\Upsilon)$$
$$\lambda_{0,1}^{hi} = \Gamma\lambda_{0,0}^{hi}$$
$$\lambda_{1,0}^{hi} = \Pi\lambda_{0,0}^{hi}$$
$$\lambda_{1,1}^{hi} = \mathrm{B}\lambda_{0,0}^{hi}$$

Where Υ is the sum of the probabilities of having a transmission event with each risk and intervention sub-group (when mixing is random and dependent on the relative number of transmission events supplied by different risk groups) with each probability multiplied by the prevalence of infection in that sub-group:

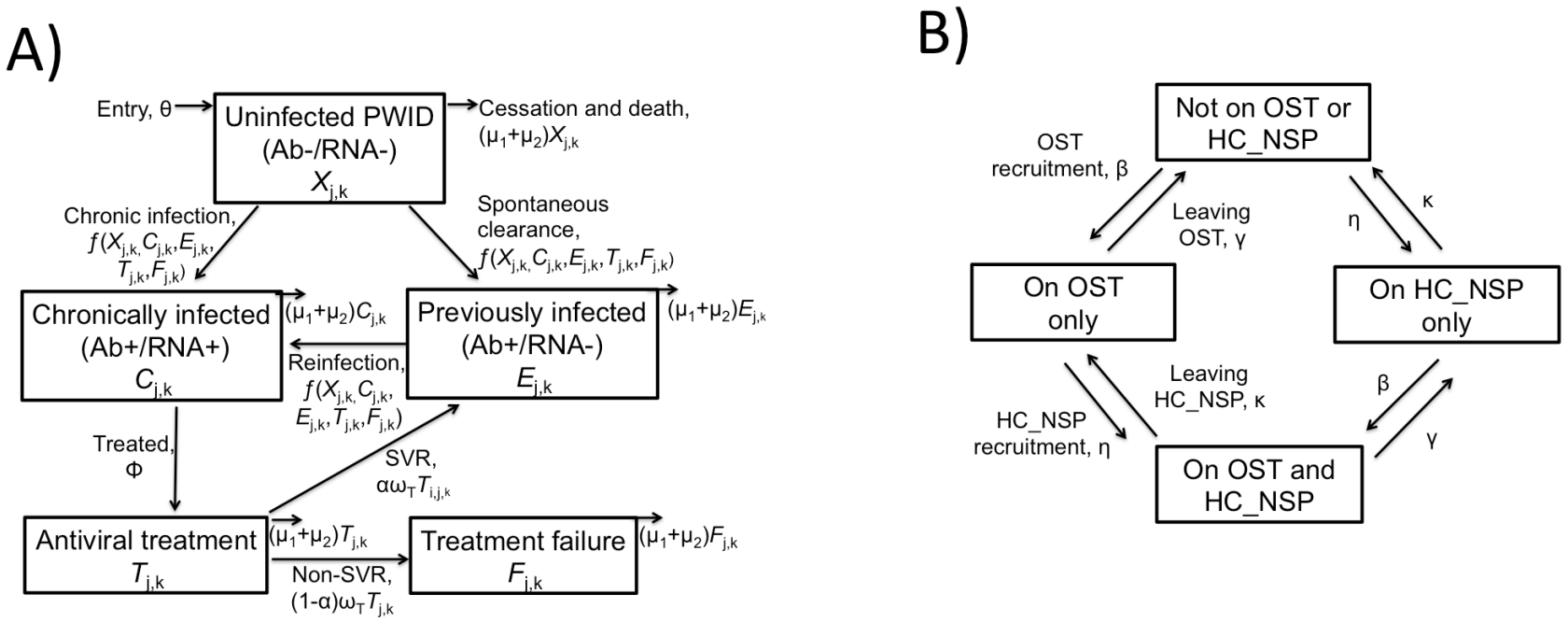
$$\Upsilon = \frac{(\Omega_{0,0}^{lo} + \Xi\Omega_{0,0}^{hi} + \Gamma(\Omega_{0,1}^{lo} + \Xi\Omega_{0,1}^{hi}) + \Pi(\Omega_{1,0}^{lo} + \Xi\Omega_{1,0}^{hi}) + \mathrm{B}(\Omega_{1,1}^{lo} + \Xi\Omega_{1,1}^{hi})}{\Omega_{0,0}^{lo} + \Lambda_{0,0}^{lo} + \Xi\Omega_{0,0}^{hi} + \Xi\Lambda_{0,0}^{hi} + \Gamma(\Omega_{0,1}^{lo} + \Lambda_{0,1}^{lo} + \Xi\Omega_{0,1}^{hi} + \Xi\Lambda_{0,1}^{hi}) + \Pi(\Omega_{1,0}^{lo} + \Lambda_{1,0}^{lo} + \Xi\Omega_{1,0}^{hi} + \Xi\Lambda_{1,0}^{hi}) + \mathrm{B}(\Omega_{1,1}^{lo} + \Lambda_{1,1}^{lo} + \Xi\Omega_{1,1}^{hi} + \Xi\Lambda_{1,1}^{hi})}$$

In addition, Ψ_{lo} and Ψ_{hi} are calculated similarly but are the sum of probabilities of having a transmission event with each intervention sub-group, given that they only have transmission events with low or high risk PWIDs, respectively, with each probability multiplied by the prevalence of infection in that sub-group:

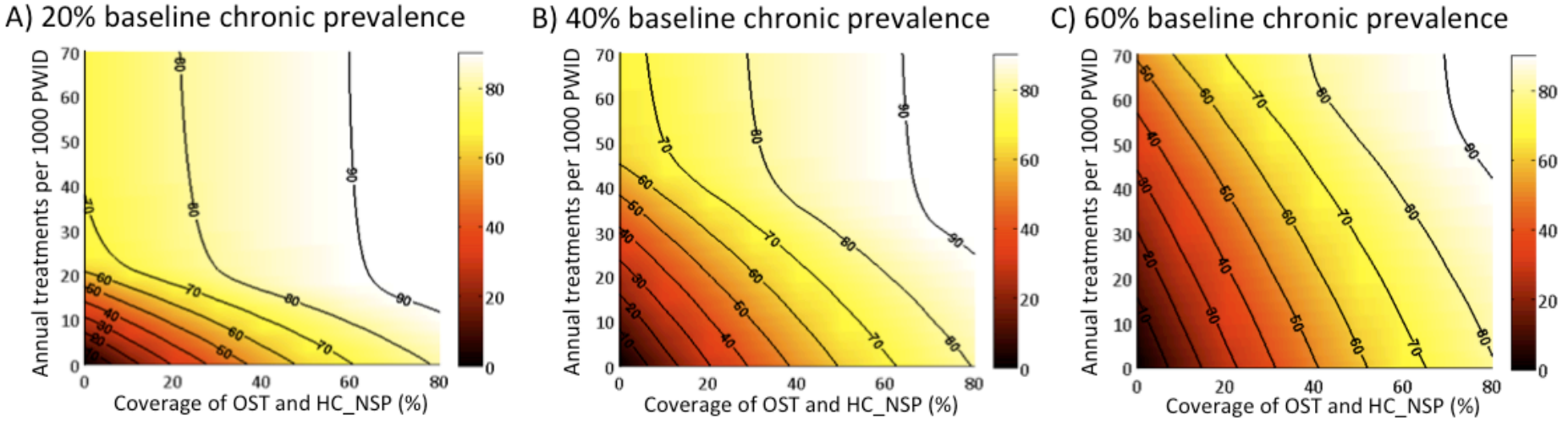
$$\Psi_{lo} = \frac{(\Omega_{0,0}^{lo} + \Gamma\Omega_{0,1}^{lo} + \Pi\Omega_{1,0}^{lo} + \Gamma\Pi\Omega_{1,1}^{lo}}{\Omega_{0,0}^{lo} + \Lambda_{0,0}^{lo} + \Gamma(\Omega_{0,1}^{lo} + \Lambda_{0,1}^{lo}) + \Pi(\Omega_{1,0}^{lo} + \Lambda_{1,0}^{lo}) + \mathrm{B}(\Omega_{1,1}^{lo} + \Lambda_{1,1}^{lo})}$$

$$\Psi_{hi} = \frac{(\Xi\Omega_{0,0}^{hi} + \Gamma\Xi\Omega_{0,1}^{hi} + \Pi\Xi\Omega_{1,0}^{hi} + \Gamma\Pi\Xi\Omega_{1,1}^{hi})}{\Xi\Omega_{0,0}^{hi} + \Xi\Lambda_{0,0}^{hi} + \Gamma(\Xi\Omega_{0,1}^{hi} + \Xi\Lambda_{0,1}^{hi}) + \Pi(\Xi\Omega_{1,0}^{hi} + \Xi\Lambda_{1,0}^{hi}) + \mathrm{B}(\Xi\Omega_{1,1}^{hi} + \Xi\Lambda_{1,1}^{hi})}$$

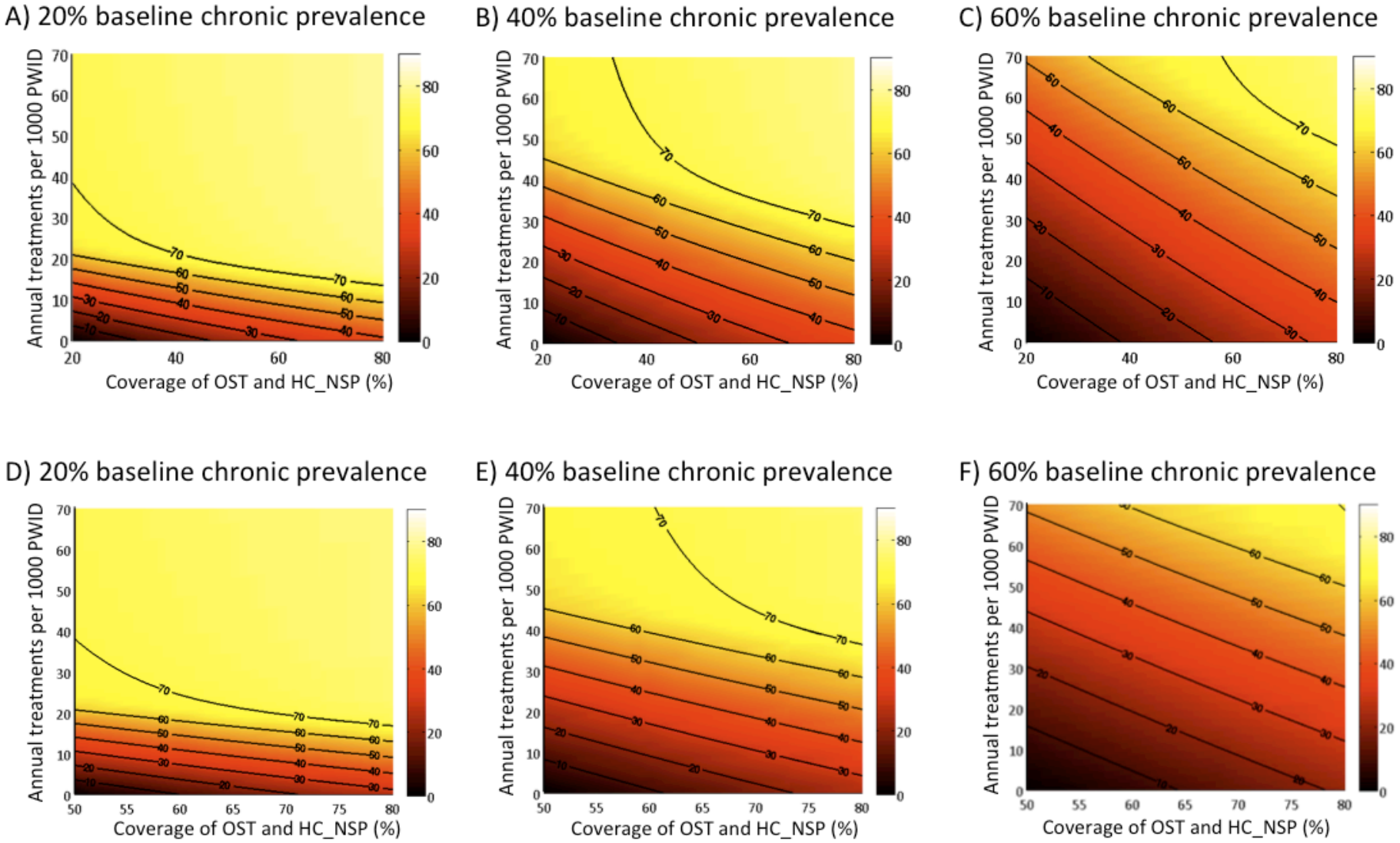
Supplementary figure 1. **Model schematic showing the HCV disease transmission and treatment states (A) and behavioral states (B).** The model includes compartments for uninfected PWID ($X_{j,k}$), chronically infected PWID ($C_{j,k}$), PWID on antiviral treatment ($T_{j,k}$), previously infected PWID ($E_{j,k}$), and PWID treatment failures ($F_{j,k}$) (**A**). Additionally, the population was stratified by intervention coverage: off/on HC_NSP (j=0 or 1, respectively), and off/on OST (k=0 or 1, respectively) (**B**). New PWID enter the model at a constant rate (θ) as uninfected, not on OST or HC_NSP. Uninfected PWID can become acutely infected with HCV and a proportion (δ) spontaneously clear their acute infection and move to the previously infected ($E_{j,k}$) compartment. The remainder (1-δ) progress to chronic infection, where they are eligible for antiviral treatment. If treated, a proportion (α) achieve SVR after a treatment duration (1/ω) and move to the previously infected ($E_{j,k}$) compartment where they are at risk of reinfection. Those who do not attain SVR (1-α) move to the treatment failure compartment where they cannot be retreated. PWID exit all compartments due to permanent cessation of drug use (μ_1) or death due to drug or non-drug related causes (μ_2). The base-case analysis assumed PWID transition between all intervention (OST/NSP) stages. More details in **appendix**. PWID=people who inject drugs, SVR=sustained viral response, OST=opiate substitution therapy, HC_NSP= high coverage needle and syringe programmes, defined as obtaining one or more sterile syringes from a NSP for each injection reported per month.



Supplementary figure 2. Contour maps of the relative reductions in incidence (%) at 10 years with various combinations of peg-IFN+RBV antiviral treatment (y axis), OST and HC_NSP (x axis) scale-up with baseline levels of OST and HC_NSP. Results are shown for three baseline chronic prevalence settings (20, 40, and 60%) with no baseline coverage of any intervention. Figures show the reductions projected using the median estimates for efficacy of OST, HC_NSP, and peg-IFN+RBV from **table 1**. PWID=people who inject drugs, SVR=sustained viral response, OST=opiate substitution therapy, HC_NSP= high coverage needle and syringe programmes, defined as obtaining one or more sterile syringes from a NSP for each injection reported per month.



Supplementary figure 3. Contour maps of the relative reductions in prevalence (%) at 10 years with various combinations of peg-IFN+RBV antiviral treatment (y axis), OST and HC_NSP (x axis) scale-up with baseline levels of OST and HC_NSP. Results are shown for three baseline chronic prevalence settings (20, 40, and 60%) with a baseline coverage of OST and HC_NSP of 20% of each (**A-C**) or 50% of each (**D-F**).Figures show the reductions projected using the median estimates for efficacy of OST, HC_NSP, and peg-IFN+RBV from **table 1**. PWID=people who inject drugs, SVR=sustained viral response, OST=opiate substitution therapy, HC_NSP= high coverage needle and syringe programmes, defined as obtaining one or more sterile syringes from a NSP for each injection reported per month.



Supplementary figure 4. Sensitivity analysis of the impact of exit rate and risk heterogeneity on the model projections with a 40% baseline HCV chronic prevalence and no interventions at baseline. (A) The combinations of interventions (OST, HC_NSP, peg-IFN+RBV) required to reduce prevalence by 50% within 10 years, given different exit rates**. (B)** The relative prevalence reductions at 10 years (y-axis) given a variety of exit rates (x-axis) with strategies using only antiviral treatment (grey dashed line), only OST and HC_NSP (black dashed line), or a combination of antiviral treatment, OST, and HC_NSP (solid black line) which achieve a 30% relative reduction in prevalence for the base-case scenario (exit rate=0.085). **(C)** The combinations of interventions where the intervention impact is not affected by variation in the exit rate. **(D)** The combinations of interventions (OST, HC_NSP, peg-IFN+RBV) required to reduce prevalence by 50% within 10 years, including a high risk group comprising 50% of the PWID population with no turnover between high/low risk, and risk ratios of 2-fold relative risk (RR) for the high risk group with proportional mixing, 6-fold RR with proportional mixing, and 6-fold RR with partially assortative mixing (50%). Figures show the reductions projected using the median estimates for efficacy of OST, HC_NSP, and peg-IFN+RBV from **table 1**. RR=relative risk, PWID=people who inject drugs, SVR=sustained viral response, OST=opiate substitution therapy, HC_NSP= high coverage needle and syringe programmes, peg-IFN+RBV= pegylated interferon and ribavirin, RR10= relative prevalence reduction at 10 years.