Supplementary Information for: Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe

Authors: Hannah Fraser; Natasha K Martin; Henrikki Brummer-Korvenkontio; Patrizia Carrieri; Olav Dalgard; John Dillon; David Goldberg; Sharon Hutchinson; Marie Jauffret-Roustide; Martin Kåberg; Amy A Matser; Mojca Matičič; Havard Midgard; Viktor Mravcik; Anne Øvrehus; Maria Prins; Jens Reimer; Geert Robaeys; Bernd Schulte; Daniela K van Santen; Ruth Zimmermann; Peter Vickerman; Matthew Hickman.

Contents:

1. Mathematical model

We used an adapted mathematical model based on previous modelling which stratifies PWID according to intervention status (on or off OST and NSP, (1)) and infection status (2) to model HCV transmission amongst PWID. The model (Figure 1a in the main paper) includes compartments for susceptible PWID ($S_{i,j}$), chronically infected PWID (antibody positive and RNA positive, $I_{i,j}$), previously infected PWID (antibody positive and RNA negative who are susceptible to re-infection, $E_{i,j}$), PWID on antiviral treatment ($T_{i,j}$) and PWID who have failed treatment ($F_{i,j}$). The model is also stratified by OST/NSP status; off/on OST ($i = 0$ or 1 resepctively) and off/on NSP ($j = 0$ or 1 respectively).

All PWID enter the model as susceptible at rate θ and become infected at a per capita rate (force of infection $\lambda_{i,j}$) which is elevated by a fixed multiplicative cofactor dependent on OST and NSP status (Γ if on OST only, Π if on NSP only, and B if on OST and NSP). Once infected, PWID either spontaneously clear infection at rate δ and transition to the previously infected group or transition to the chronically infected state at rate $(1 - \delta)$. The group of PWID that are previously infected are antibody positive and therefore can be re-infected, again either transitioning to the chronically infected state or spontaneously clearing the infection and remaining in the group they are in. We do not model acute infection because previous modelling has shown it contributes little to transmission (1, 3). Chronically infected PWID can be treated; after treatment (which has duration $1/\omega$) a proportion (α) attain a sustained viral response (SVR) and PWID transition to the previously infected group at rate where they can again become infected. However, if SVR is not attained (proportion $(1 - \alpha)$) PWIDs transition to the treatment failure group. In the baseline model treatment failures are not retreated, however once modelling the new Direct Acting Antivirals (DAAs) retreatment of those

that fail treatment is included. We do not include any type of immunity to re-infection following treatment or spontaneous clearance as evidence is unclear about whether the rate of reinfection following spontaneous clearance(4) or treatment(5, 6) is higher or lower than the rate of primary infection, and previous modelling has shown immunity to have little effect on model projections(4, 7, 8). We assume that the risk of infection is proportional to HCV chronic prevalence and do not assume a risk different after treatment. PWID leave the model from every group through either ceasing injecting or through HCV or unrelated mortality.

The model is also stratified by OST/NSP status (Figure 1b in the main paper). All PWID enter the model with no coverage of OST or NSP, and transition onto OST and NSP at rates β and η respectively. PWID stop OST and NSP at rates γ and κ respectively. Further information on how these rates are calibrated are given in the next section.

The full model equations for sites which model **opioid injection only** (Amsterdam, Belgium, Denmark, France, Hamburg, Norway, Scotland and Slovenia) are given by

For PWID not on OST or NSP

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

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

$$\frac{dI_{0,0}}{dt} = (1-\delta)\lambda_{0,0}\left(S_{0,0}+E_{0,0}\right) - \Phi^{1}_{0,0}(t) + \gamma I_{1,0} + \kappa I_{0,1} - (\beta+\eta+\mu_1+\mu_2)I_{0,0}$$

$$\frac{dT_{0,0}}{dt} = \Phi^{1}_{0,0}(t) + \Phi^{2}_{0,0}(t) - \omega T_{0,0} + \gamma T_{1,0} + \kappa T_{(0,1)} - (\beta+\eta+\mu_1+\mu_2)T_{0,0}$$

$$\frac{dF_{0,0}}{dt} = (1-\alpha)\omega T_{0,0} - \Phi^{2}_{0,0}(t) + \gamma F_{1,0} + \kappa T_{0,1} - (\beta+\eta+\mu_1+\mu_2)F_{0,0}$$

For PWID on OST and not on NSP

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

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

$$\frac{dI_{1,0}}{dt} = (1-\delta)\lambda_{1,0}\left(S_{1,0}+E_{1,0}\right) - \Phi^{1}_{(1,0)}(t) + \beta I_{0,0} + \kappa I_{1,1} - (\gamma+\eta+\mu_1+\mu_2)I_{1,0}$$

$$\frac{dT_{1,0}}{dt} = \Phi^{1}_{1,0}(t) + \Phi^{2}_{1,0}(t) - \omega T_{1,0} + \beta T_{0,0} + \kappa T_{1,1} - (\gamma+\eta+\mu_1+\mu_2)T_{1,0}$$

$$\frac{dF_{1,0}}{dt} = (1-\alpha)\omega T_{1,0} - \Phi^{2}_{1,0}(t) + \beta F_{0,0} + \kappa F_{1,1} - (\gamma+\eta+\mu_1+\mu_2)F_{1,0}$$

For PWID not on OST and on NSP

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

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

$$\frac{dI_{0,1}}{dt} = (1-\delta)\lambda_{0,1}\left(S_{0,1} + E_{0,1}\right) - \Phi^1_{0,1}(t) + \eta I_{0,1} + \gamma I_{1,1} - (\kappa + \beta + \mu_1 + \mu_2)I_{0,1}$$

$$\frac{dT_{0,1}}{dt} = \Phi^1_{0,1}(t) + \Phi^2_{0,1}(t) - \omega T_{0,1} + \eta T_{0,1} + \gamma T_{1,1} - (\kappa + \beta + \mu_1 + \mu_2)T_{0,1}$$

$$\frac{dF_{0,1}}{dt} = (1-\alpha)\omega T_{0,1} - \Phi^2_{0,1}(t) + \eta F_{0,1} + \gamma F_{1,1} - (\kappa + \beta + \mu_1 + \mu_2)F_{0,1}$$

For PWID on both OST and NSP

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

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

$$\frac{dI_{1,1}}{dt} = (1-\delta)\lambda_{1,1}\left(S_{1,1} + E_{1,1}\right) - \Phi^1_{1,1}(t) + \eta I_{1,0} + \beta I_{0,1} - (\kappa + \gamma + \mu_1 + \mu_2)I_{1,1}$$

$$\frac{dT_{1,1}}{dt} = \Phi^1_{1,1}(t) + \Phi^2_{1,1}(t) - \omega T_{1,1} + \eta T_{1,0} + \beta T_{0,1} - (\kappa + \gamma + \mu_1 + \mu_2)T_{1,1}$$

$$\frac{dF_{1,1}}{dt} = (1-\alpha)\omega F_{1,1} - \Phi_{1,1}^{2}(t) - \eta T_{1,0} + \beta_{T(0,1)} - (\kappa + \gamma + \mu_1 + \mu_2)F_{1,1}$$

where the force of infection is given by

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

$$\lambda_{1,0} = \Gamma\lambda_{0,0}$$

$$\lambda_{0,1} = \Pi\lambda_{0,0}$$

$$\lambda_{1,1} = \mathrm{B}\lambda_{0,0}$$

where

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

and

$$\Lambda_{i,j} = S_{i,j} + E_{i,j} + \alpha T_{i,j}.$$

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

For sites where **only those on OST are treated** (Amsterdam, Belgium, Denmark, Finland, France, Hamburg, Scotland, Slovenia) at baseline the treatment rates are given by

$$\Phi^1_{1,j}(t) = \begin{cases} 0 \; if \; t < tStart \\ \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1}} \; if \; \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1}} < I_{1,j} \; and \;\; t \geq tStart \\ I_{1,j} if \; \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1}} \geq I_{1,j} \; and \; t \geq tStart \end{cases}$$

and

$$\Phi^2_{1,j}(t) = 0 \; \forall \; t$$

When switching to direct acting antivirals for sites where only those on OST are treated the treatment rates are given by

$$\Phi_{1,j}^{1}(t) = \begin{cases} 0 \; if \; t < t_1 \\ \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1}} \; if \; \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1}} < I_{1,j} \; and \; t_1 \leq t < 2016 \\ I_{1,j} if \; \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1}} \geq I_{1,j} \; and \; t_1 \leq t < 2016 \\ \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1} + F_{1,0} + F_{1,1}} \; if \; \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1} + F_{1,0} + F_{1,1}} < I_{1,j} \; and \; t \geq 2016 \\ I_{1,j} \; if \; \phi \dfrac{I_{1,j}}{I_{1,0} + I_{1,1} + F_{1,0} + F_{1,1}} \geq I_{1,j} \; and \; t \geq 2016 \end{cases}$$

and

$$\Phi_{1,j}^{2}(t) = \begin{cases} 0 \; if \; t < 2016 \\ \phi \dfrac{F_{1,j}}{I_{1,0} + I_{1,1} + F_{1,0} + F_{1,1}} \; if \; \phi \dfrac{F_{1,j}}{I_{1,0} + I_{1,1} + F_{1,0} + F_{1,1}} < F_{1,j} \; and \; t \geq 2016 \\ F_{1,j} \; if \; \phi \dfrac{F_{1,j}}{I_{1,0} + I_{1,1} + F_{1,0} + F_{1,1}} \geq F_{1,j} \; and \; t \geq 2016 \end{cases}$$

All other treatment rates ($\Phi_{0,j}^{1}(t)$ and $\Phi_{0,j}^{2}(t)$) are equal to zero.

In Norway, where a proportion of treatments are amongst those on OST and a proportion are amongst those not on OST when switching to direct acting antivirals the treatment rates are given by

$$\Phi_{i,j}^{1}(t) = \begin{cases} 0\ if\ t < t_1 \\ r\phi \dfrac{I_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1}}\ if\ r\phi \dfrac{I_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1}} < I_{i,j}\ and\ \ t_1 \le t < 2016 \\ I_{i,j} if\ r\phi \dfrac{I_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1}} \ge I_{i,j}\ and\ t_1 \le t < 2016 \\ r\phi \dfrac{I_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1} + F_{0,0} + F_{1,0} + F_{1,1} + F_{1,1}}\ if\ r\phi \dfrac{I_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1} + F_{0,0} + F_{1,0} + F_{1,1} + F_{1,1}} < I_{i,j}\ and\ t \ge 2016 \\ I_{i,j}\ if\ r\phi \dfrac{I_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1} + F_{0,0} + F_{1,0} + F_{1,1} + F_{1,1}} \ge I_{i,j}\ and\ t \ge 2016 \end{cases}$$

and

$$\Phi_{i,j}^{2}(t) = \begin{cases} 0\ if\ t < 2016 \\ r\phi \dfrac{F_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1} + F_{0,0} + F_{1,0} + F_{1,1} + F_{1,1}}\ if\ r\phi \dfrac{F_{i,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1} + F_{0,0} + F_{1,0} + F_{1,1} + F_{1,1}} < F_{i,j}\ and\ t \ge 2016 \\ F_{i,j}\ if\ r\phi \dfrac{F_{1,j}}{I_{0,0} + I_{1,0} + I_{0,1} + I_{1,1} + F_{0,0} + F_{1,0} + F_{1,1} + F_{1,1}} \ge F_{i,j}\ and\ t \ge 2016 \end{cases}$$

where $r = r_1$ is the proportion treated who are on OST when $i = 1$ and $r = (1 - r_1)$ when $i = 0$.

We include **both opioid and methamphetamine injecting** for Czech Republic, Finland and Sweden, and therefore the model equations differ slightly for these two sites. In this case as well as the equations given above for those injecting opioids there are a further 10 equations given by

For PWID injecting methamphetamine not on NSP

$$\frac{dS_{0,0}^{M}}{dt} = \theta_2 - \lambda_{0,0}^{M} S_{0,0}^{M} + \kappa S_{0,1}^{M} - (\eta + \mu_1 + \mu_3) S_{0,0}^{M}$$

$$\frac{dE_{0,0}^{M}}{dt} = \delta \lambda_{0,0}^{M} S_{0,0}^{M} - (1-\delta) \lambda_{0,0}^{M} E_{0,0}^{M} + \alpha \omega T_{0,0}^{M} + \kappa E_{0,1}^{M} - (\eta + \mu_1 + \mu_3) E_{0,0}^{M}$$

$$\frac{dI_{0,0}^{M}}{dt} = (1-\delta) \lambda_{0,0}^{M} \left(S_{0,0}^{M} + E_{0,0}^{M}\right) - \Phi_{0,0}^{1\mathrm{M}}(t) + \kappa I_{0,1} - (\eta + \mu_1 + \mu_3) I_{0,0}^{M}$$

$$\frac{dT_{0,0}^{M}}{dt} = \Phi_{0,0}^{1\mathrm{M}}(t) + \Phi_{0,0}^{2M}(t) - \omega T_{0,0}^{M} + \kappa T_{(0,1)}^{M} - (\eta + \mu_1 + \mu_3) T_{0,0}^{M}$$

$$\frac{dF_{0,0}^{M}}{dt} = (1-\alpha) \omega T_{0,0}^{M} - \Phi_{0,0}^{2M}(t) + \kappa T_{0,1} - (\eta + \mu_1 + \mu_3) F_{0,0}^{M}$$

For PWID injecting methamphetamine and on NSP

$$\frac{dS_{0,1}^{M}}{dt} = -\lambda_{0,1}^{M} S_{0,1}^{M} + \eta S_{0,0} - (\kappa + \mu_1 + \mu_3) S_{0,1}^{M}$$

$$\frac{dE_{0,1}^{M}}{dt} = \delta\lambda_{0,1}^{M}S_{0,1}^{M} + (1-\delta)\lambda_{0,1}^{M}E_{0,1}^{M} + \alpha\omega T_{0,1}^{M} + \eta E_{0,1}^{M} - (\kappa + \mu_1 + \mu_3)E_{0,1}^{M}$$

$$\frac{dI_{0,1}^{M}}{dt} = (1-\delta)\lambda_{0,1}^{M}\left(S_{0,1}^{M} + E_{0,1}^{M}\right) - \Phi_{0,1}^{1M}(t) + \eta I_{0,1}^{M} - (\kappa + \mu_1 + \mu_3)I_{0,1}$$

$$\frac{dT_{0,1}^{M}}{dt} = \Phi_{0,1}^{1M}(t) + \Phi_{0,1}^{2M}(t) - \omega T_{0,1}^{M} + \eta T_{0,1}^{M} - (\kappa + \mu_1 + \mu_3)T_{0,1}^{M}$$

$$\frac{dF_{0,1}^{M}}{dt} = (1-\alpha)\omega T_{0,1}^{M} - \Phi_{0,1}^{2M}(t) + \eta F_{0,1}^{M} - (\kappa + \mu_1 + \mu_3)F_{0,1}^{M}$$

We assume random mixing between opioid and methamphetamine injectors. Therefore, the force of infection is given by

$$\lambda_{0,0} = \frac{\Omega_{0,0} + \Omega_{0,0}^{M} + \Gamma\Omega_{1,0} + \Pi(\Omega_{0,1} + \Omega_{0,1}^{M}) + \mathrm{B}\Omega_{1,1}}{\Omega_{0,0} + \Lambda_{0,0} + \Omega_{0,0}^{M} + \Lambda_{0,0}^{M} + \Gamma\left(\Omega_{1,0} + \Lambda_{1,0}\right) + \Pi(\Omega_{0,1} + \Lambda_{0,1} + \Omega_{0,1}^{M} + \Lambda_{0,1}^{M}) + \mathrm{B}(\Omega_{1,1} + \Lambda_{1,1})}$$

$$\lambda_{1,0} = \Gamma\lambda_{0,0}$$

$$\lambda_{0,1} = \Pi\lambda_{0,0}$$

$$\lambda_{1,1} = \mathrm{B}\lambda_{0,0}$$

where $\Omega_{i,j} = I_{i,j} + (1-\alpha)T_{i,j} + F_{i,j}$ and $\Lambda_{i,j} = S_{i,j} + E_{i,j} + \alpha T_{i,j}$, $\Omega_{i,j}^{M} = I_{i,j}^{M} + (1-\alpha)T_{i,j}^{M} + F_{i,j}^{M}$ and $\Lambda_{i,j}^{M} = S_{i,j}^{M} + E_{i,j}^{M} + \alpha T_{i,j}^{M}$.

In Czech Republic and Sweden it is assumed all chronically infected PWID can be treated. Therefore, when switching to DAAs, a similar expression for treatment is used as for Norway, however the proportion r is removed and the infected and failed treatment compartments are included in the numerator and denominator as appropriate.

2. Model calibration

The model was parameterised to each of the 11 sites based on previously published research (Tables 1-12). Site-specific data for duration of injecting, mortality rate, proportion genotype 1, SVR rates for the different genotypes and new DAAs, and treatment numbers were used to parameterise the model.

For each site, 2500 model parameter sets were randomly sampled from the parameter uncertainty distributions (Tables S1a-S1l). The rate of initiating injecting was fitted (using the built in Matlab function lsqnonlin) to fit to a PWID population size of 1000 which was used for all sites. The recruitment rates onto OST and NSP were also fit using lsqnonlin to achieve the required sampled coverages at each site. Finally, the transmission rate was fit such that the fitted chronic or antibody prevalence required at the specific year for each site was achieved.

For Czech Republic, Finland and Sweden a similar process was taken, with 2,500 parameter sets randomly sampled from the parameter uncertainty distributions alongside HCV prevalence estimates. However, for each parameter set the model was then fit to the PWID population

size in each sub-group (opioid and meth/amphetamine injectors) by varying two recruitment rates, to OST coverage by varying recruitment onto OST amongst opioid injectors, to NSP coverage by varying the recruitment rates of both sub-groups onto NSP and to either chronic or antibody HCV prevalence at a site-specific time-point by varying the transmission rate, which is the same for both sub-groups.

For Amsterdam, 3,500 parameter sets were randomly sampled, and two recruitment rates were fitted to fit to the decreasing PWID population size between 2009 and 2014, after which the PWID population is assumed stable. We fit to both chronic prevalence and incidence and assumed a decrease in transmission rate between 2009 and 2015. From these 3,500 parameter sets, runs were excluded if the second recruitment rate was un-realistically small, leaving a sample of 2,492 on which all analyses have been performed.

Detailed information on the parameters for each site are given in Supplementary Tables S1a-S1k. Any ranges that are given were sampled in each of the parameter runs, and the distribution sampled from given in the tables. For normal distributions, if the sample size was known this was used to estimate the 95% confidence interval. However, if we had a range we assumed this was the 95% confidence interval and sampled from a normal distribution within this range. The model was run using MATLAB 2016a, using timesteps of 0.05 year.

Supplementary Tables S1a:S1k: Detailed information regarding parameter ranges for each of the 11 sites. Table S1l gives parameter ranges which were constant among sites.

Supplementary Table S1a: Amsterdam

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	Median 16 IQR 6-24[a]	Uniform	Data from the Amsterdam Cohort Studies (data not published)	
Mortality rate	23.7/1000	Poisson	(9)	2006-2012
Proportion genotype 1	69.2% (47.1 – 86.8)	Normal	(10)	Sample size: 23. HCV Genotype Distribution Among Seropositive Young Drug Users in Amsterdam Over Time
SVR genotype 1	37.5% (26.3 – 48.8%)	Normal	(11)	Small sample size (16) so +/- 30%
SVR genotype 2/3	76% (68.4 – 83.6%)	Normal	(11)	Sample size: 41
PWID population size	2621 (1946-3374) in 2009 1874 (1341-2455) in 2014	Normal	(12)	Model a decreasing population size.
Antibody prevalence	51% (44.1-57.0%)	Normal	Data from the Amsterdam Cohort Study (data not published)	Sample size: 218
Year prevalence calibrated to	2014			
Treatment starts	2005		(13)	Based on data from PWID from Amsterdam
Number treated per year	15		(13)	Based on data from PWID from Amsterdam
OST coverage	75% (52.5 – 97.5%)	Normal	(14)	+/- 30%.

				"Of the opioid drug-using population, roughly 75% regularly use methadone, as opposed to approximately 40% ten years ago [13,14]. Some use methadone on a regular basis, others only occasionally"
NSP coverage	50% (35-65%)	Normal		
Duration on OST	1yr			

[a] Treatment interruption not taken into account

Supplementary Table S1b: Belgium

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	12.4yrs (6.2 – 18.6yrs)	Uniform	(15)	+/-50%
Mortality rate	25 per 1000	Poisson	(16, 17)	
Proportion genotype 1	43.7% (31.9 – 56.0%)	Normal	(16)	Sample size: 71
SVR genotype 1	65.2% (42.7 – 83.6%)	Normal	(16)	Sample size: 23
SVR genotype 2/3	92% (74 – 92%)	Normal	(16)	Sample size: 25 Have taken upper bound as 92%.
PWID population size	9080 (6356 – 11804)	Normal	(17)	+/-30%
Antibody prevalence	43.3% (34.3 – 52.4%)	Normal	(18)	
Year prevalence calibrated to	2012		(18)	
Treatment starts	2004			
Number treated per year	30 per year		(16)	
OST coverage	35.6% (27.4 – 50.8%)	Log-normal	(17)	3230 on OST. Then use PWID population estimates.

NSP coverage	29.6% (22.8 –42.3%)	Log-normal	(17)	2690 using NSP. Then use PWID population estimates.
Duration on OST	3.7 yrs		(16)	

Supplementary Table S1c: Czech Republic

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	Opioid: 12yrs (6 – 18yrs) Methamphetamine: 9yrs (4.5 – 13.5yrs)	Uniform	(19)	+/-50%
Mortality rate	7.5 per 1000	Poisson	(20-22)	Give 0.7-0.8. As use Poisson distribution have used mid point.
Proportion genotype 1	75.5% (69.5 – 81.2%)	Normal	(23)	Sample size: 222 Note this is for Prague.
SVR genotype 1	53.8% (45.3 – 62.2%)	Normal	(24)	Sample size: 143 Note this is for Brno
SVR genotype 2/3	82.1% (63.1 – 93.9%)	Normal	(24)	Sample size: 28 Note this is for Brno
PWID population size	41816 – 46563	Normal	(25)	
Antibody prevalence	35% (31.6 – 38.5%)	Normal	(26, 27)	National HCV study in low threshold facilities
Year prevalence calibrated to	2004		(26)	Study 2003-2005
Treatment starts	2002		(28)	
Number treated per year	2002-2011: 370 per year 2011-2015: 540 per year		(27-29)	

OST coverage	32% (22 – 41.6%)	Normal	(27)	Estimated 3000-4000 users in OST of 10700 estimated opioid problem users. Taken as 3500 gives 32%. Then have +/- 30%.
NSP coverage	70% (49 – 91%)	Normal	(27)	
Duration on OST	0.93 yr		(30)	Calculated from substitution register in Czech Republic.
Ratio of opioid:methamphetamine injectors	1:3		(25)	

Supplementary Table S1d: Denmark

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	12 year (IQR 7 – 19yrs)[a]	Uniform	(31)	From a survey investigating prevalence of chronic hepatitis and HIV unfection among drug users attending treatment centres. Median time since first injection.
Mortality rate	20/1000 per year	Poisson	(32, 33)	
Proportion genotype 1	45.9% (40.9 – 51.0%)	Normal	H. Krarup perss comm with Anne	Sample size: 6000 National numbers of all infected
SVR genotype 1	44.4% (35.8-53.2)	Normal	(34)	No genotypic SVR rates available for IDUs.
SVR genotype 2/3	71.9% (66.3-77.1)	Normal	(34)	

				G1: 59/133 G2/3: 205/285
PWID population size	16500 (13000 – 19000)	Normal	(35-37)	The Danish Health Board estimates 13.000 (10.066-16.821) people are active injectors based on a cross reference between the National Patient Register and the National Drug Treatment Register(SIB). (P. Christensen 2009) 7850 patients are registered in SIB (2012) to be on OST. A proportion are still injecting By cross referencing the different databases where a diagnosis of Chronic hepatitis C can be found with information from SIB about the proportion of PWIDS tested and the proportion positive it is estimated that there is aprox. 9.500 drugs users (all kinds) with CHC (diagnosed and undiagnosed). From the same and other studies it is estimated that 40- 53% of all PWIDS have CHC(anti HCV 67-85% - 62,2 % develops CHC). This would correspond to a total "PWID number" of 19.000.(35, 36, 38).

Chronic prevalence	35 – 45%	Normal	Mössner et al J Med Virology 2010 Øvrehus et al Poster Inshu 2015	Mössneret al J Med Virology 2010 1635-39 (40% 2009 data – sample Øvrehus et al Poster Inshu 2015 2015 sample n= 411 35%
Year prevalence calibrated to	2014		Personal communication with Anne Øvrehus	
Treatment starts	2002			
Number treated per year	2002-2014: 53 per yr 2014-2015: 50 per yr 2015-2016: 100		(34). Personal communication with Anne Øvrehus	432 registered treatments in the national treatment database DANHEP 2002-2007. 219 infected by IDU, Aprox under reporting 20% (219*1.2)/5 = 53 Treated if on OST.
OST coverage	41.1 – 60%	Log-normal	National drug treatment register	Currently 7800 on OST. The calculated based on PWID pop size.
NSP coverage	50% (35-65%)	Normal		+/- 30% No data for Denmark
Duration on OST	1 yr			

[a] Note this is median time since first injection, not necessarily duration of injection.

Supplementary Table S1e: Finland

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	14yrs (7 – 21yrs)	Uniform	Unpublished – 2014 exit poll bio-behaviour study.	+/- 50% Sample size 600.
Mortality rate	2%	Poisson	(39)	Western Europe
Proportion genotype 1	25.1% (24.0 – 26.2%)	Normal	(40)	
SVR genotype 1	50-60%	Normal	(40)	

SVR genotype 2/3	70-80%	Normal	(40)	
PWID population size	15611 (13770 – 22655)	Normal	(41)	
Antibody prevalence	76% (72.4-79.4%)	Normal	Unpublished – 2014 exit poll bio-behaviour study.	Sample size 600.
Year prevalence calibrated to	2014			
Treatment starts	2006		Number treated per year 5 (active injecting drug users). This is an average estimate for the past 10 years. Communication with Henrikki Brummer-Korvenkontio	
Number treated per year	5			
OST coverage	24.4-28.1%	Normal	Best expert opinion. (42)	
NSP coverage	68% (47.2 - 77.6%)	Log-normal	Annual data collection from Low Threshold Service Centres (Needle Exchange) by National Institute for Health and Welfare (THL).	
Duration on OST	5 yrs		(43)	

Supplementary Table S1f: France

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	14yrs (7 – 21yrs)	Uniform	ANRS-coquelicot	
Mortality rate	1.26%	Poisson	Mortality cohort OFDT	
Proportion genotype 1	46% (32.3 – 59.8%)	Normal	ANRS-Hepavih	+/- 30%
SVR genotype 1	70-75%	Normal	ANRS-Hepavih	+/- 10%
SVR genotype 2/3	80%	Normal	ANRS-Hepavih	
PWID population size	80000 (65000 – 95000)	Normal	(44) OFDT	

Antibody prevalence	66.37% (60.32 – 71.92%)	Normal	(45) ANRS-coquelicot	Sample size: 418
Year prevalence calibrated to	2011		ANRS-coquelicot	
Treatment starts	2001			
Number treated per year			(45) ANRS-coquelicot Treatment amongst those on OST. Note: these are the calculated number treated Treatment number is treatment rate given on 52% of PWID who are antibody positive.	Sample size: 291 Treatment number calculated based on finding the proportion PWID who are antibody positive that have not been cured and then using the treatment rate (6.2% (3.0-12.3%)) to find the number treated each year.
OST coverage	80%	Normal		+/- 10%
NSP coverage	40 – 60%	Normal		
Duration on OST	1 yr.			

Supplementary Table S1g: Hamburg

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	18 yrs IQR: 12-24yrs	Uniform	(46)	
Mortality rate	0.73 per yr	Poisson	(47)	
Proportion genotype 1	52.1% (46.4 – 57.6%)	Normal	(46) Details of survey methodology: (48)	Sample size: 319
SVR genotype 1	48% (34.7 – 62.0%)	Normal	(49)	Confidence bounds for both calculated using stata. N=56 for G1/4
SVR genotype 2/3	81% (66.9 – 90.2%)	Normal	(49)	

				N=51 for G2/3
PWID population size	8492 (7582 – 9436)	Normal	(50) Estimates on the basis of OST registration data: On July 1, 2013: 4.246 patients registered for OST in Hamburg. OST coverage estimates among problem opiate user ranges between 45%-56% (Kraus et al. 2004; RKI 2014)	
Antibody prevalence	67.7% (62.3 -72.8)	Normal	(46)	Sample size: 319
Year prevalence calibrated to	2014		(49)	
Treatment starts	2005		Communication with Bernd Schulte	
Number treated per year	2005-2011: 60 per yr 2011-2015: 72 per yr		"Own calculations of prescription data from the Northern Germany Computing Centre for Pharmacies. For the calculations we used the prescription data of Methadone/Buprenorphin to identify patients in OST (N=3691 for 2011) for the region of Hamburg. For those OST patients,we identified 72 co-prescriptions of PEG-IFN and/or Ribavirin for the year 2011."	
OST coverage	56.3% (50.8-61.9%)	Normal	(46)	
NSP coverage	78.5% (73.4-82.8%)	Normal	(51, 52) Reported number of PWID receiving 'needle and syringes' at low-threshold facilities in the last 30days acoording to a question of the Druck-study for Hamburg (Question: Reported main	Sample size: 319

			source/location for needle/syringe exchange)	
Duration on OST	24.93 months		Calculated for this study. Used a dataset from 2005-2011.	

Supplementary Table S1h: Norway

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	14yrs (7 – 21yrs)	Uniform	(53)	
Mortality rate	1.9% per year	Poisson	(54)	
Proportion genotype 1	40% (28% - 52%)	Normal	Norwegian Institute of Public Health	
SVR genotype 1	45% (24.4 – 65.1%)	Normal	(55)	Sample size: 25
SVR genotype 2/3	70% (55.4 – 82.1%)	Normal	(55)	Sample size: 50
PWID population size	15500 (10850 – 20150)	Normal	(56) and data on file based on Norwegian Prescription Registry (OST 2004-2014)	+/- 30%
Chronic prevalence	45% (42.6 – 47.5%)	Normal	Surveillance data from Oslo and Bergen. Rikard Rykkvin, National Insitute of Health.	Sample size: 1639. Prevalence 45% Bounds found using stata
Year prevalence calibrated to	2007			Data for 2002-2012 so taken half way point.
Treatment starts	2009			
Number treated per year	100 per yr		(57) + personal communication with Olav Dalgard	
OST coverage	40% (28% - 52%)	Normal	(58)	
NSP coverage	51% (35-73%)	Normal	Personal communication Ellen Amundsen, Norwegian Intitute of Public Health	
Duration on OST	1.97 yrs		(59)	

Supplementary Table S1i: Scotland

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	11yrs (5.5 – 16.5yrs)	Uniform	(60)	+/- 50%
Mortality rate	1% per year	Poisson	(61)	
Proportion genotype 1	47.8% (46.9 – 48.6%)	Normal	(62)	
SVR genotype 1	39.0 (33.6 – 44.7%)	Normal	(63)	
SVR genotype 2/3	69.7% (65.8 – 73.4%_)	Normal	(63)	
PWID population size	16000 (11500 – 19400)	Normal	(64)	
Antibody prevalence	58% (55.8 – 60.2%)	Normal	NESI	
Year prevalence calibrated to	2013/14		NESI	
Treatment starts	2005		Communication with Sharon Hutchinson	
Number treated per year	2005-2008: 60 per yr 2008-2009: 90 per yr 2009-2015: 150 per yr		Communication with Sharon Hutchinson	
OST coverage	54.5% (51.4 – 57.8%)	Normal	NESI	
NSP coverage	77% (75.2 – 78.8%)	Normal	(65)	Sample size: 2154. 77% coverage. Bounds found using stata
Duration on OST	2/3rd of a year (240 days)		(66)	

Supplementary Table S1j: Slovenia

Parameter	Value	Distribution	Reference	Notes

Duration of injecting	15.4yrs (7.7-23.1 yrs)	Uniform		Average taken for sites +/- 50%
Mortality rate	0.26% per yr	Poisson	(67)	
Proportion genotype 1	38.6% (36.1 – 41.1%)	Normal	(68)	Sample size 1504
SVR genotype 1	75% (55 – 89%)	Normal	(69, 70)	Total sample size 130. 28% G1 – n=36 72% G3 – n=94 Bound upper estimate for G2/3 with mean as high.
SVR genotype 2/3	87.5% (79.1 – 87.5%)	Normal		
PWID population size	6000 (4200 - 7800)	Normal	(67)	+/- 30%
Antibody prevalence	27.3% (19.1 – 35.5%)	Normal	(67)	+/- 30%
Year prevalence calibrated to	2012		(67)	
Treatment starts	1997		(69)	
Number treated per year	1997-1999: 2 per yr 1999-2008: 5 per yr 2008-2015: 62 per yr		(69-72)	
OST coverage	43% (30 – 56%)	Normal		+/- 30% No data for Slovenia
NSP coverage	50% (35-65%)	Normal		+/- 30% No data for Slovenia
Duration on OST	1yr			

Supplementary Table S1k: Sweden

Parameter	Value	Distribution	Reference	Notes
Duration of injecting	17.8yrs (8.9 – 26.7yrs)	Uniform	Stockholm Needle Exchange Programme	+/-50%

Mortality rate	2%	Poisson	(39)	Western Europe
Proportion genotype 1	54.3% (42.9 – 65.4%)	Normal	(73)	Sample size: 81 Note this is for three Swedish cities.
SVR genotype 1	42.9% (17.5–68.2%)	Normal	(74)	Using systematic review as sample size so small
SVR genotype 2/3	73.1% (55.2–91.0%)	Normal	(74)	Using systematic review as sample size so small
PWID population size	8021 - 26550	Normal	(75-77)	8021 – estimated number of PWID in 2008-2011. Probable underestimate. Maximum is 90% of the Estimated number of "problematic drug users" (PDU), defined as people who inject drugs during the past 12 months or have used illicit drugs on a daily basis during the past
Antibody prevalence	81.7% (79.6 – 83.6%)	Normal	Stockholm Needle Exchange Programme	N = 1507
Year prevalence calibrated to	2014			
Treatment starts	2014		Communication with Martin Kaberg	
Number treated per year	2004-2013: 45 2014: 0 2015: 70 (new DAAs)		(73) Communication with Martin Kaberg	
OST coverage	14 – 46%	Normal	Ref for 3700 on OST: (78), personal communication Martin Kaberg	3700 people on OST (2013). Percentages found based on max and min population sizes.

NSP coverage	9.8-32%	Normal	Communication with Martin Kaberg	In 2014 only 2592 persons visited the Sweden NSPs http://www.regeringen.se/contentassets/4a81589e331641eaa4ecec35c714347f/okad-tillganglighet-till-sprututbytesverksamheter-i-sverige-ds-2015_56-webb.pdf
Duration on OST	1yr			
Ratio of opioid:methamphetamine injectors	1:1		Communication with Martin Kaberg	Largest NSP cohort.

Supplementary Table S1l: All other parameters

Parameter	Value	Distribution	Reference	Notes
Rate of spontaneous clearance	0.26 (0.22-0.29)	Normal	(79)	
Relative risk of acquiring HCV while:				
on OST	0.42 (0.3-0.53)	Log-normal	(80)	
on NSP	0.43 (0.15-0.70)	Log-normal	(80)	
on OST and NSP	0.18 (0.04-0.32)	Log-normal	(80)	
SVR rate new DAAs	0.9 (0.85-0.95)	Normal	(81, 82)	
Average treatment duration (pre-DAA treatment):				
Genotypes 1 failed treatment	12 weeks		(83)	Weighted average calculated from

Genotype 1	48 weeks		(83)	Proportion G1*Duration G1 + Proportion G2/G3*Duration G2/G3. Duration G1 calculated from G1_svr*Duration SVR + (1-G1_svr)*Duration non SVR
Genotypes 2/3	24 weeks		(83)	
All genotypes new DAAs	12 weeks		(81, 82)	

3. Results

Table S2a and S2b shows the median and 95% credibility intervals for the 2,500 parameter sets for the chronic prevalence (S1a) and incidence per 100 person years (S2b) in 2016, chronic prevalence in 2026 if switching to DAAs, switching and doubling treatments and switching and treating 50 per 1000 PWID annually. The table also shows the relative decrease in chronic prevalence between 2016 and 2026. For each site the top row shows these metrics with current coverage of OST and NSP at each site, and the bottom row shows if OST and NSP are increased to 80% coverage (unless coverage is already higher).

Table S3 shows the differential benefit of scaling-up OST and NSP alongside treatment on reducing chronic prevalence compared to current OST and NSP levels. For each site, the tables shows the relative decrease in HCV prevalence between 2016 and 2026 if treatment is scaled-up with current levels of OST and NSP and with scaled-up OST and NSP to 80% coverage when switching to DAAs, and how much fold greater this difference is.

Table S2a: Table showing HCV chronic prevalence at baseline in 2016 and under the different scenarios in 2026 both with and without the scale-up of OST and NSP to 80% coverage if not already achieved. The relative decrease between 2016 and 2026 in chronic HCV prevalence is also given. Values are the median and 95% credibility interval

Site	With/without scale-up of OST/NSP	HCV chronic prevalence				Relative decrease 2016 - 2026		
		2016	2026 – switch to DAAs	2026 – Switch and double treatment	2026 – Switch to DAA and treat 50/1000 PWID	Switch to DAAs	Switch and double treatments	Switch and treat 50/1000 PWID
Amsterdam	Without	33.0% (29.0-37.4%)	15.8% (10.6-25.2%)	14.5% (9.3-23.8%)	0.1% (0.0-0.5%)	51.8% (28.7-65.7%)	55.8% (32.8-69.6%)	99.7% (98.4-99.9%)
	With	33.0% (29.0-37.4%)	14.4% (9.7-23.0%)	13.1% (8.5-21.6%)	0.1% (0-0.2%)	56.4% (35.0-68.4%)	60.2% (39.0-72.3%)	99.8% (99.5-100.0%)
Belgium	Without	31.6% (25.6-37.5%)	30.2% (23.9-36.3%)	27.6% (21.2-34.3%)	9.7% (4.9-14.7%)	4.4% (2.2-8.0%)	11.6% (7.2-18.9%)	69.3% (57.5-83.3%)
	With	31.6% (25.6-37.5%)	16.2% (10.0-23.7%)	14.0% (8.1-21.4%)	0.2% (0.1-0.5%)	48.4% (31.2-65.7%)	55.6% (38.6-72.3%)	99.5% (98.7-99.9%)
Czech Republic	Without	20.9% (18.2-23.8%)	13.0% (9.3-16.8%)	1.8% (0.3-6.2%)	<0.1%	37.8% (28.2-49.8%)	91.6% (73.5-98.2%)	99.9% (99.7-99.9%)
	With	20.9% (1.2-23.8%)	9.2% (5.0-13.7%)	0.6% (0.1-3.2%)	<0.1%	55.8% (39.7-74.7%)	97.3% (86.1-99.4%)	99.9% (99.8-100.0%)
Denmark	Without	39.9% (35.6-44.1%)	36.7% (32.0-41.3%)	32.5% (27.3-37.6%)	6.3% (3.5-10.9%)	7.6% (5.2-10.8%)	18.1% (13.1-24.5%)	84.1% (74.7-90.6%)
	With	39.9% (35.6-44.1%)	22.3% (15.5-29.1%)	18.1% (11.6-24.8%)	0.5% (0.2-1.3%)	43.5% (29.9-59.6%)	54.2% (40.6-69.5%)	98.7% (96.9-99.4%)
Finland	Without	56.1% (53.1-59.4%)	56.1% (53.0-59.4%)	56.0% (52.9-59.2%)	24.8% (18.2-31.5%)	0.1% (0.1-0.2%)	0.4% (0.3-0.6%)	55.9% (46.1-66.2%)
	With	56.2%	46.3%	46.1%	12.8%	17.6%	17.9%	77.3%

		(53.1-59.4%)	(40.0-51.6%)	(39.8-51.5%)	(5.9-20.0%)	(10.0-27.9%)	(10.3-28.2%)	(65.8-89.1%)
France	Without	47.3% (42.3-51.9%)	43.9% (35.6-50.2%)	30.0% (6.6-41.8%)	24.9% (11.6-39.4%)	6.7% (2.3-18.1%)	36.4% (16.7-85.5%)	47.6% (21.7-73.8%)
	With	47.3% (42.3-51.9%)	30.5% (19.2-39.9%)	14.2% (1.0-29.8%)	8.3% (2.1-21.0%)	35.5% (19.7-57.5%)	69.7% (39.2-97.8%)	82.5% (57.3-95.4%)
Hamburg	Without	49.6% (45.7-53.5%)	45.8% (41.4-50.3%)	40.0% (34.9-45.0%)	13.9% (8.2-20.8%)	7.5% (5.3-10.1%)	19.3% (15.2-24.3%)	71.9% (60.5-82.4%)
	With	49.6% (45.7-53.5%)	39.9% (34.4-45.7%)	33.8% (28.2-39.9%)	7.4% (3.1-14.5%)	19.5% (11.7-27.6%)	31.7% (23.0-40.7%)	81.9% (72.3-93.3%)
Norway	Without	42.9% (40.7-45.2%)	40.0% (36.7-42.9%)	35.8% (31.0-39.5%)	8.1% (4.1-13.3%)	6.7% (4.2-10.8%)	16.5% (11.3-25.1%)	81.1% (70.0-90.1%)
	With	42.9% (40.7-45.2%)	24.3 (17.1-30.8%)	19.8% (12.7-26.6%)	0.5% (0.2-1.3%)	43.3% (28.8-59.4%)	53.6% (38.4-70.1%)	98.9% (97.0-99.6%)
Scotland	Without	42.3% (40.2-44.7%)	38.5% (35.3-41.7%)	32.4% (27.3-36.8%)	8.1% (4.5-14.9%)	8.9% (5.6-13.9%)	23.5% (16.1-33.8%)	80.8% (66.1-89.0%)
	With	42.3% (40.2-44.7%)	29.3% (23.0-35.1%)	22.7% (16.3-29.2%)	1.8% (0.8-5.0%)	30.8% (18.1-45.2%)	46.3% (32.4-61.2%)	95.8% (88.4-98.0%)
Slovenia	Without	16.2% (10.7-21.7%)	8.2% (0.8-15.4%)	0.4% (0.0-7.3%)	<0.05%	48.8% (28.0-92.7%)	97.4% (65.5-99.9%)	99.9% (99.8-100.0%)
	With	16.2% (10.7-21.7)	3.4% (0.1-8.6%)	0.1% (0.0-1.7%)	<0.05%	78.6% (57.3-99.0%)	99.5% (91.8-99.9%)	100.0% (99.9-100.0%)
Sweden	Without	60.0% (57.4-62.9%)	58.9% (55.8-62.1%)	56.8% (52.5-60.4%)	31.3% (25.1-38.0%)	1.8% (1.1-3.8%)	5.2% (3.3-10.4%)	47.9% (38.6-57.2%)
	With	60.0% (57.4-62.9%)	41.4% (34.1-47.8%)	38.7% (31.1-45.6%)	9.9% (3.6-17.3%)	31.1% (21.6-42.8%)	35.5% (25.3-47.9%)	83.5% (72.1-93.9%)

Table S2b: Table showing HCV incidence per 100 person years at baseline in 2016 and under the different scenarios in 2026 both with and without scale-up of OST and NSP to 80% coverage if not already achieved. The relative decrease between 2016 and 2026 in chronic HCV prevalence is also given. Values are the median and 95% credibility interval

Site	With/without scale-up of OST/NSP	HCV incidence per 100pyrs				Relative decrease 2016 - 2026		
		2016	2026 – switch to DAAs	2026 – Switch and double treatment	2026 – Switch to DAA and treat 50/1000 PWID	Switch to DAAs	Switch and double treatments	Switch and treat 50/1000 PWID
Amsterdam	Without	1.9 (1.1-2.7)	0.9 (0.4-1.8)	0.8 (0.4-1.7)	<0.05	52.6% (29.2-66.5%)	56.4% (33.0-70.3%)	99.7% (98.3-99.9%)
	With	1.9 (1.1-2.7)	0.5 (0.2-1.1)	0.4 (0.2-1.1)	<0.01	70.3% (50.0-82.2%)	72.9% (53.1-84.1%)	99.9% (99.6-100.0%)
Belgium	Without	7.1 (3.5-11.7)	6.8 (3.2-11.4)	6.3 (2.9-10.9)	2.4 (0.9-5.0)	4.2% (2.2-7.7%)	10.6% (6.6-17.2%)	64.4% (52.2-79.8%)
	With	7.1 (3.5-11.7)	1.4 (0.8-2.7)	1.2 (0.6-2.4)	<0.05	78.9% (63.8-89.7%)	81.8% (68.1-91.5%)	99.8% (99.3-99.9%)
Czech Republic	Without	5.6 (3.3-8.4)	3.5 (1.8-6.0)	0.5 (0.1-2.1)	<0.05	37.8% (28.2-49.7%)	91.6% (78.5-98.2%)	99.9% (99.7-99.9%)
	With	5.6 (3.3-8.4)	2.0(0.8-4.2)	0.1 (0.0-0.9)	<0.05	62.0% (42.6-82.8%)	97.7% (86.7-99.5%)	99.9% (99.8-100.0%)
Denmark	Without	10.7 (6.4-15.9)	9.9 (5.8-15.0)	8.8 (5.0-13.7)	1.9 (0.8-4.2)	7.3% (5.0-10.3%)	17.4% (12.6-23.4%)	82.3% (72.3-89.5%)
	With	10.7 (6.4-15.9)	3.1 (1.7-5.7)	2.5 (1.4-4.8)	0.1 (0.0-0.2)	69.5% (51.5-83.0%)	75.1% (59.3-87.2%)	99.2% (97.9-99.7%)
Finland	Without	19.8 (13.3-27.1)	19.7 (13.3-27.0)	19.7 (13.2-26.9)	8.5 (4.6-14.0)	0.1% (0.1-0.2%)	0.5% (0.3-0.6%)	57.0% (47.6-66.7%)

	With	19.8 (13.3-27.1)	11.5 (7.5-17.0)	11.5 (7.4-17.0)	3.2 (1.2-6.4)	41.0% (26.1-57.6%)	41.2% (26.4-57.8%)	83.4% (72.3-93.3%)
France	Without	17.0 (9.5-26.2)	15.9 (8.4-25.4)	10.7 (2.4-19.5)	9.5 (2.9-20.8)	5.9% (2.0-16.0%)	33.2% (15.0-83.1%)	44.0% (19.2-70.6%)
	With	17.0 (9.5-26.2)	7.4 (3.8-14.6)	3.3 (0.3-9.4)	2.2 (0.4-8.0)	54.1% (32.6-74.1%)	78.5% (50.8-98.4%)	87.2% (64.6-97.0%)
Hamburg	Without	10.1 (6.9-13.6)	9.3 (6.2-12.8)	8.1 (5.3-11.5)	3.1 (1.5-5.6)	7.5% (5.6-10.0%)	19.0% (15.2-23.6%)	68.7% (57.7-80.0%)
	With	10.1 (6.9-13.6%)	3.2 (3.9-9.5)	5.2 (3.3-8.3)	1.2 (0.4-3.0)	37.2% (19.3-53.2%)	46.5% (29.8-60.8%)	87.5% (74.9-97.6%)
Norway	Without	11.9 (7.1-17.3)	11.0 (6.5-16.4)	9.9 (5.6-15.0)	2.5 (0.9-5.4)	6.6% (4.2-10.6%)	16.1% (11.2-24.4%)	79.1% (67.4-88.9%)
	With	11.9 (7.1-17.3)	3.3 (1.9-6.2)	2.7 (1.5-5.3)	0.1 (0.0-0.2)	71.0% (52.3-83.9%)	76.2% (58.8-87.9%)	99.4% (98.0-99.8%)
Scotland	Without	13.8 (7.7-20.0)	12.6 (6.8-18.8)	10.6 (5.5-16.5)	2.8 (1.0-6.9)	8.7% (5.5-13.6%)	22.9% (15.8-33.0%)	79.5% (64.8-88.2%)
	With	13.8 (7.7-20.0)	6.8 (3.8-12.2)	5.3 (2.9-10.1)	0.4 (0.2-1.7)	48.0% (26.3-64.7%)	59.4% (39.5-74.4%)	98.7% (89.9-98.6%)
Slovenia	Without	2.6 (1.3-4.8)	1.3 (0.1-3.3)	0.1 (0.0-1.5)	<0.01	48.5% (27.7-92.6%)	97.3% (65.3-99.9%)	99.9% (99.8-100.0%)
	With	2.6 (1.3-4.8)	0.3 (0.0-0.9)	<0.5	<0.01	89.2% (73.6-99.5%)	99.7% (95.3-100.0%)	100.0%
Sweden	Without	19.9 (13.7-26.4)	19.2 (13.4-26.0)	18.5 (12.7-25.2)	10.4 (6.1-16.2)	1.8% (1.0-3.7%)	5.1% (3.2-9.9%)	46.9% (37.9-56.2%)
	With	19.6 (13.7-26.4)	6.8 (4.2-10.8)	6.4 (3.9-10.2)	1.7 (0.5-4.0)	64.6% (50.1-77.5%)	66.7% (52.3-79.0%)	91.0% (80.9-97.5%)

Table S3: Table showing relative decrease in HCV prevalence between 2016 and 2026 if switching to DAAs without and with scale-up of OST and NSP coverage to 80%, and the differential impact scaling-up OST and NSP to 80% coverage has on the relative decrease in chronic prevalence.

Site	Relative decrease in prevalence if current OST and NSP coverage	Relative decrease in prevalence if OST and NSP coverage is scaled-up to 80% coverage	Differential benefit of scaling-up OST and NSP on relative decrease
Amsterdam	51.8% (28.7-65.7%)	56.4% (35.0-68.4%)	1.1 (1.0-1.3)
Belgium	4.4% (2.2-8.0%)	48.4% (31.2-65.7%)	11.0 (4.7-25.8)
Czech Republic	37.8% (28.2-49.8%)	55.8% (39.7-74.7%)	1.4 (1.1-2.2)
Denmark	7.6% (5.2-10.8%)	43.5% (29.9-59.6%)	5.7 (3.2-9.9)
Finland	0.1% (0.1-0.2%)	17.6% (10.0-27.9%)	146.7 (67.2-312.2)
France	6.7% (2.3-18.1%)	35.5% (19.7-57.5%)	5.1 (2.1-14.4)
Hamburg	7.50% (5.3-10.1%)	19.5% (11.7-27.6%)	2.5 (1.5-4.3)
Norway	6.7% (4.2-10.8%)	43.3% (28.8-59.4%)	6.4 (3.3-12.2)
Scotland	8.9% (5.6-13.9%)	30.8% (18.1-45.2%)	3.4 (1.8-6.7)
Slovenia	48.8% (28.0-92.7%)	78.6% (57.3-99.0%)	1.6 (1.1-2.4)
Sweden	1.8% (1.1-3.8%)	31.1% (21.6-42.8%)	16.5 (7.7-32.8)

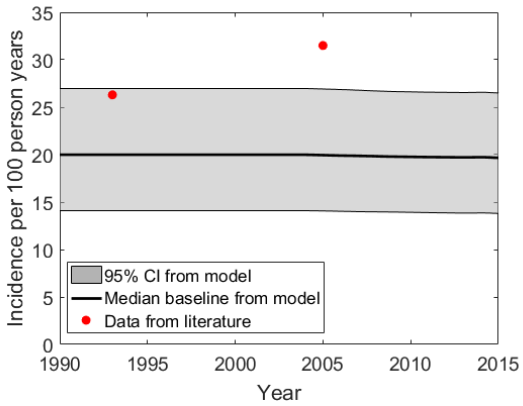
Figure S1 shows the median incidence per 100 person years among PWID in Sweden, France, Czech republic, Finland and Scotland. At each of the sites the data is comparable with the model estimates; this is especially true as some of the estimates are for cities or larger areas rather than country wide. Confidence bounds from the data are given if possible.

Figures S2 and S3 show the projected 10-year HCV incidence per 100 person years among PWID in multiple sites in Europe for different levels of scale-up of HCV treatment with new DAAs if current coverage of OST and NSP are maintained or OST and NSP are scaled-up to 80% coverage respectively.

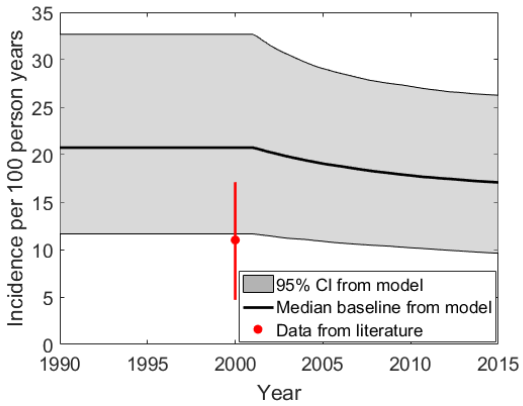
Figure S4 shows the results of the sensitivity analysis for each site. The figures show the proportion of the uncertainty each parameter contributes to the variation in the decrease in chronic prevalence and incidence between 2016 and 2026 when current treatment rates are doubled with new DAAs for each of the different sites. Note that only parameters which contribute more than 1% to the variation at each site are shown; all other parameters are grouped together.

Figure S1: Incidence per 100 person years in (a) Sweden, (b) France, (c) Czech Republic, (d) Finalnd and (e) Scotland. Figures show median and 95% credibility intervals from the 2,500 runs for each site that were fit to prevalence estimates only. The dots (and lines if data available) show the mean and 95% confidence interval from data for each of the sites.

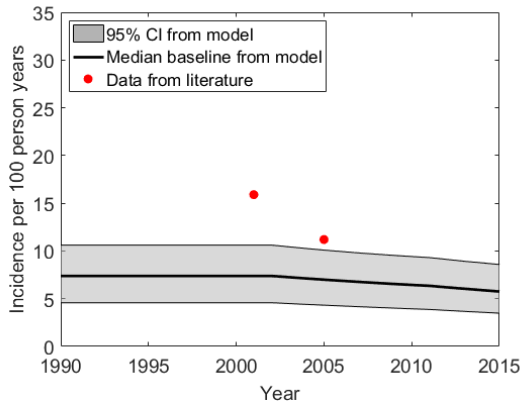
(a) Projected incidence in Sweden



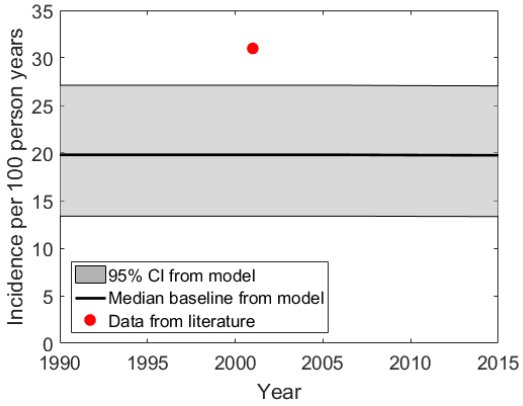
(b) Projected incidence in France



(c) Projected incidence in Czech Republic



(d) Projected incidence in Finland



(e) Projected incidence in Scotland

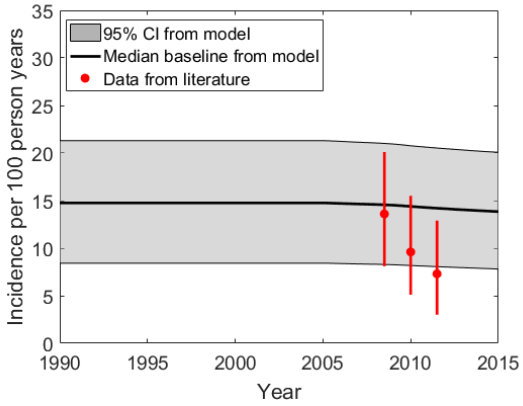


Figure S2: Baseline and projected 10 year incidence per 100 person years among PWID in multiple sites in Europe if either current treatment rates continue with new DAAs (green boxes), treatment rates are doubled (yellow boxes), or 50 per 1000 PWID are treated annually (pink boxes) with OST and NSP at current coverage. Bars indicate the median and interquartile range and whiskers show the 95% credibility intervals of the uncertainty analysis. $ z-score < 0.5 (unlikely to observe a difference between 2016 and 2026), + z-score 0.5-1.5 (may be able to observe a difference between 2016 and 2026), * z-score 1.5-3 (increasingly likely to be able to observe and difference between 2016 and 2026), #z-score >3 (highly likely to be able to observe a difference between 2016 and 2026).

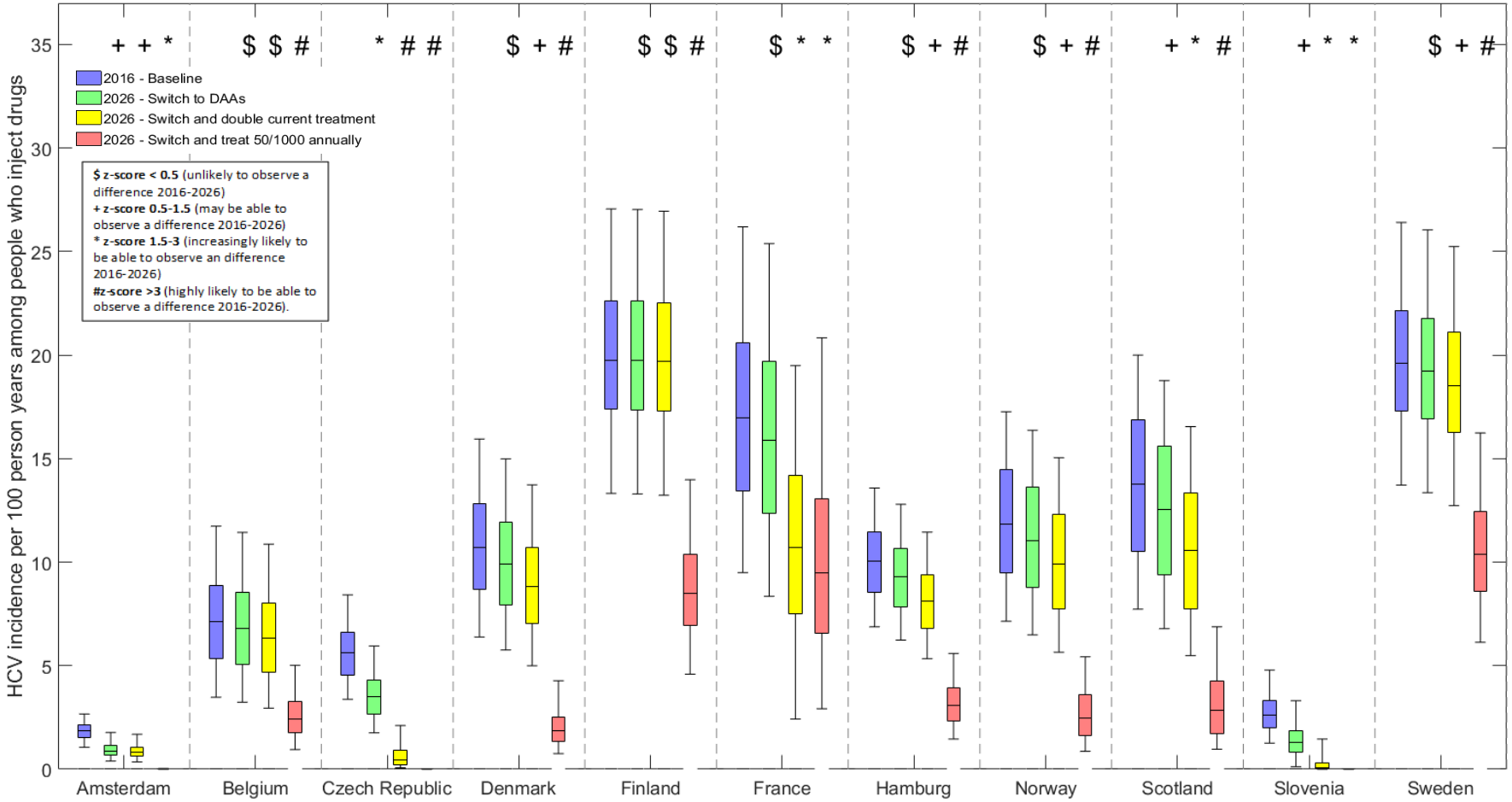


Figure S3: Baseline and projected 10 year incidence per 100 person years among PWID in multiple sites in Europe if either current treatment rates continue with new DAAs (green boxes), treatment rates are doubled (yellow boxes), or 50 per 1000 PWID are treated annually (pink boxes) with OST and NSP scaled-up to 80% coverage. Bars indicate the median and interquartile range and whiskers show the 95% credibility intervals of the uncertainty analysis. $ z-score < 0.5 (unlikely to observe a difference between 2016 and 2026), + z-score 0.5-1.5 (may be able to observe a difference between 2016 and 2026), * z-score 1.5-3 (increasingly likely to be able to observe and difference between 2016 and 2026), #z-score >3 (highly likely to be able to observe a difference between 2016 and 2026).

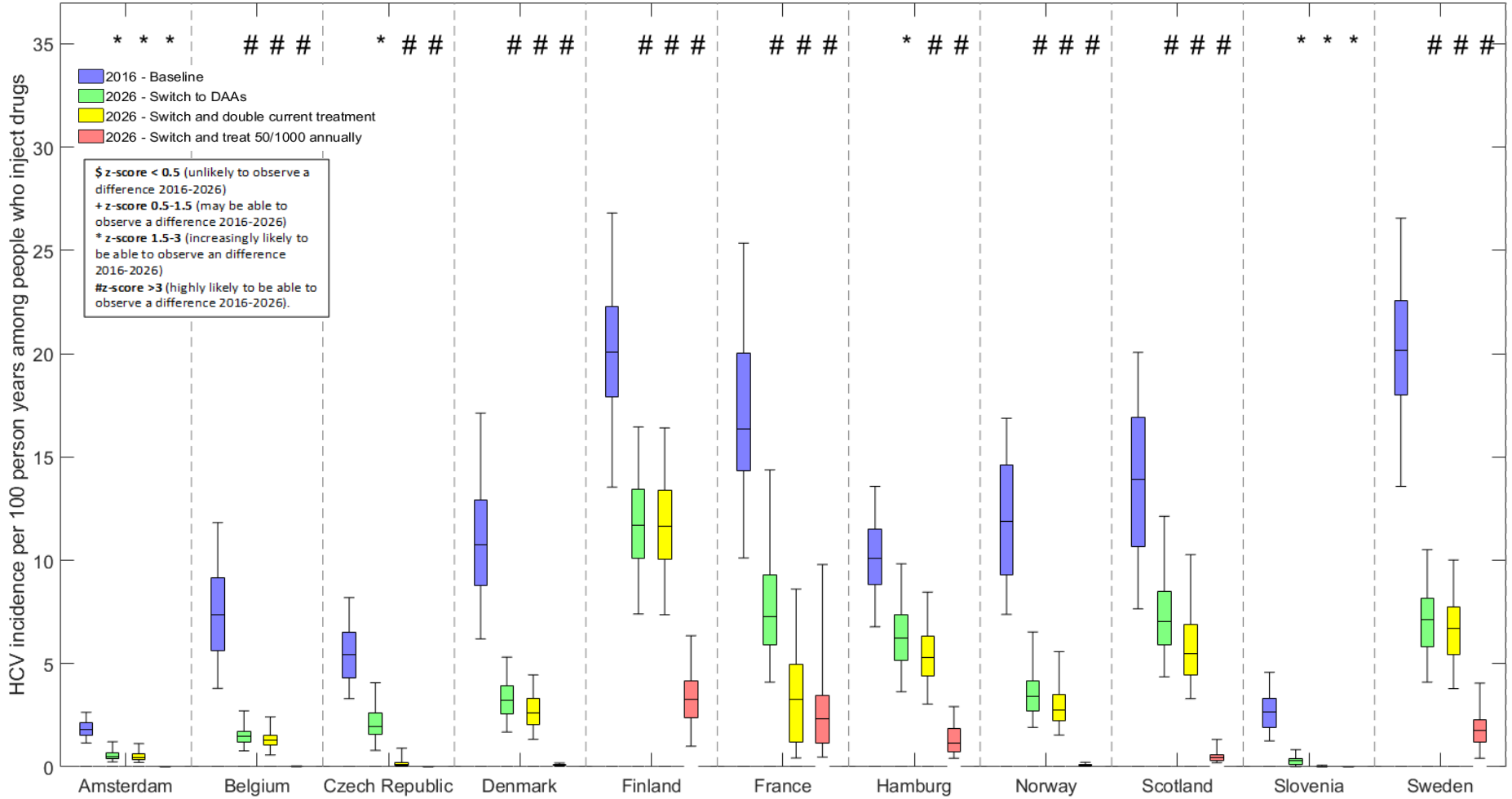
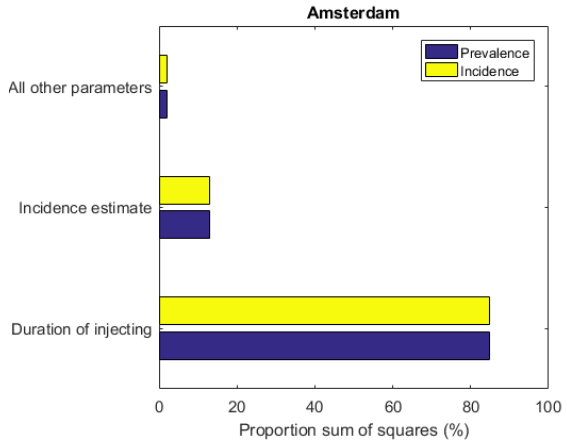
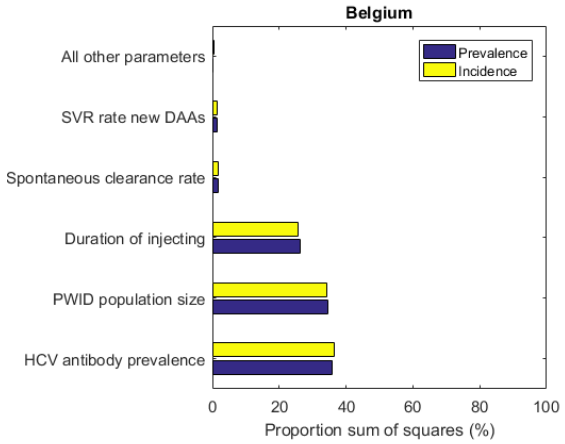


Figure S4: Results of the sensitivity analysis for each site showing the proportion of the uncertainty in relative chronic prevalence decrease and relative incidence decrease between 2016 and 2026 with OST and NSP at current coverage resulting from uncertainty in each parameter for (a) Amsterdam, (b) Belgium, (c) Czech Republic, (d) Denmark, (e) Finland, (f) France, (g) Hamburg, (h) Norway, (i) Scotland, (j) Slovenia and (k) Sweden.

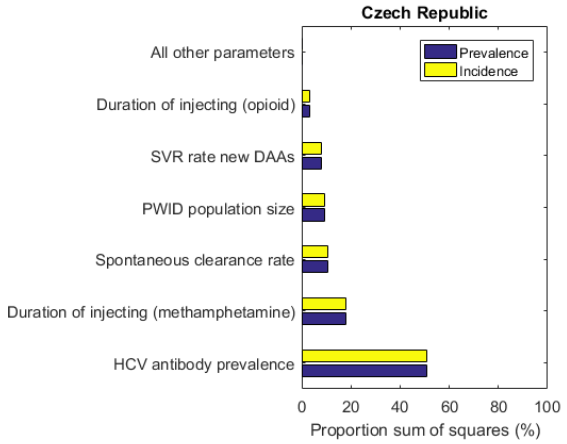
(a)



(b)



(c)



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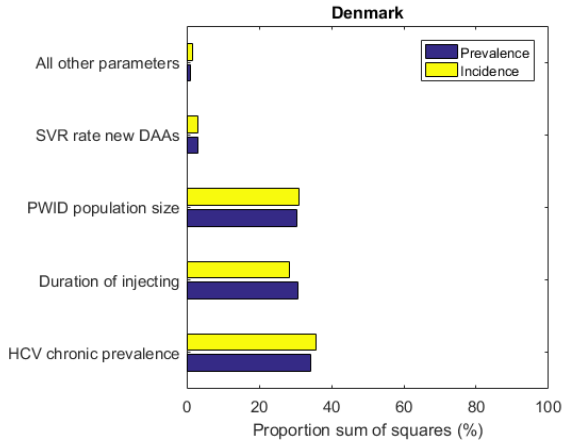

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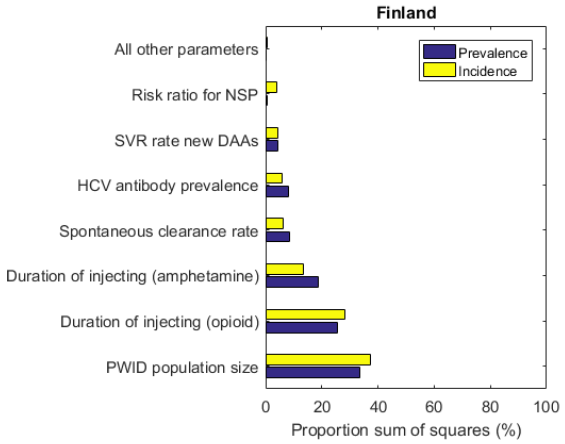

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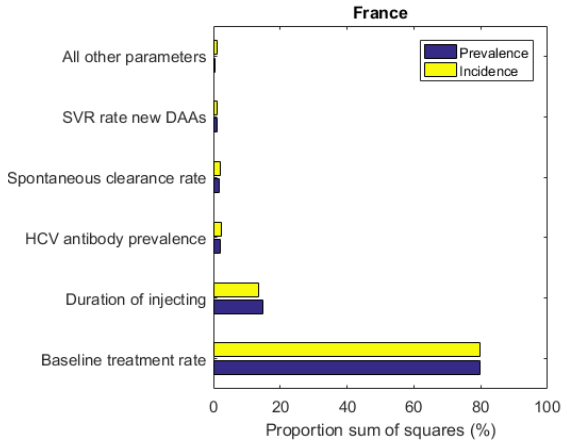
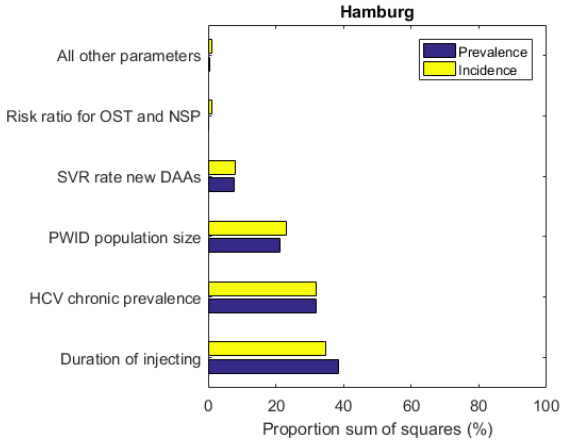


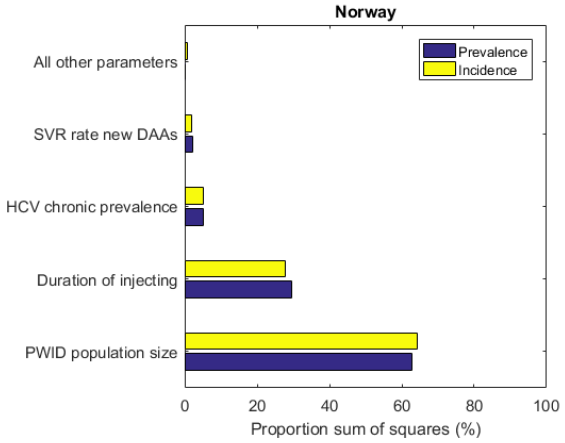
(g)

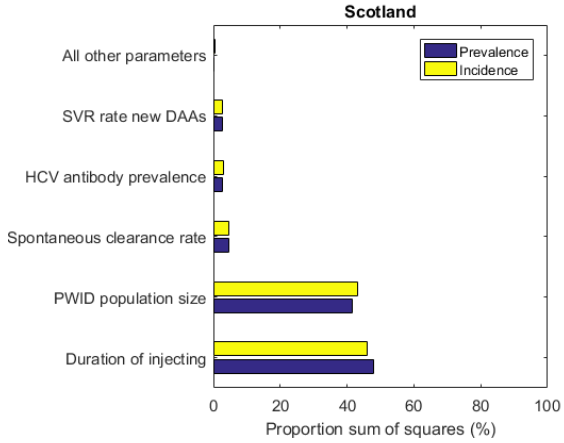
(h)

(i)

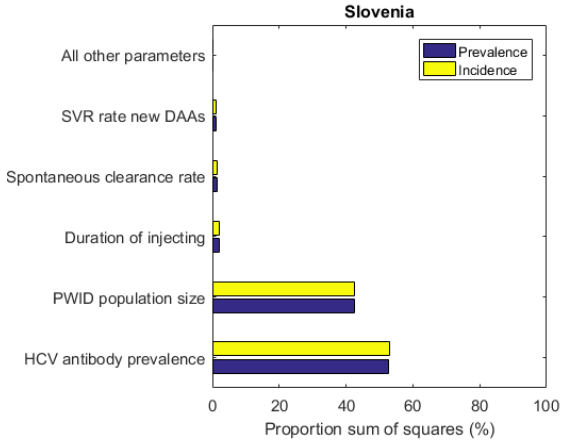

Hamburg
All other parameters
Risk ratio for OST and NSP
SVR rate new DAAs
PWID population size
HCV chronic prevalence
Duration of injecting
Prevalence
Incidence
0
20
40
60
80
100
Proportion sum of squares (%)

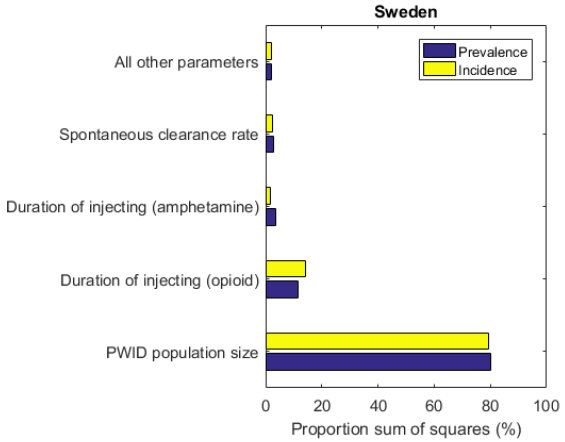
(j)


Norway
All other parameters
SVR rate new DAAs
HCV chronic prevalence
Duration of injecting
PWID population size
Prevalence
Incidence
0
20
40
60
80
100
Proportion sum of squares (%)


Scotland
All other parameters
SVR rate new DAAs
HCV antibody prevalence
Spontaneous clearance rate
PWID population size
Duration of injecting
Prevalence
Incidence
0
20
40
60
80
100
Proportion sum of squares (%)

(k)


Slovenia
All other parameters
SVR rate new DAAs
Spontaneous clearance rate
Duration of injecting
PWID population size
HCV antibody prevalence
Prevalence
Incidence
0
20
40
60
80
100
Proportion sum of squares (%)


Sweden
All other parameters
Spontaneous clearance rate
Duration of injecting (amphetamine)
Duration of injecting (opioid)
PWID population size
Prevalence
Incidence
0
20
40
60
80
100
Proportion sum of squares (%)

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