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

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Published in:
Journal of Hepatology

DOI:
10.1016/j.jhep.2017.10.010

Publication date:
2018

Document Version
Author accepted manuscript

Link to publication in ResearchOnline

Citation for published version (Harvard):
Fraser, H, Martin, NK, Brummer-Korvenkontio, H, Carrieri, P, Dalgard, O, Dillon, J, Goldberg, D, Hutchinson, S, Jauffret-Roustide, M, Kåberg, M, Matser, AA, Maticic, M, Midgard, H, Mravcik, V, Øvrehus, A, Prins, M, Reimer, J, Robaeys, G, Schulte, B, van Santen, DK, Zimmermann, R, Vickerman, P & Hickman, M 2018, 'Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe', *Journal of Hepatology*, vol. 68, no. 3, pp. 402-411. https://doi.org/10.1016/j.jhep.2017.10.010

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Download date: 04. Dec. 2022

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

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Funding: The study was funded by European Commission Drug Prevention and Information Programme (DIPP) [JUST/2013/DPIP/AG/4812]. In addition we acknowledge support from the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Evaluation of Interventions at the University of Bristol in partnership with Public Health England. NM, PV, and MH were supported by the National Institute for Drug Abuse [grant number R01 DA037773-01A1]. NM was additionally supported by the University of California San Diego Center for AIDS Research(CFAR)), a National Institute of Health (NIH) funded program [grant number P30 AI036214]

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health or Public Health England.

VM: institutional support no. PRVOUK-P03/LF1/9 and the project Nr. LO1611 with a financial support from the MEYS under the NPU I program.

Disclosures: NM,MH,PV has received unrestricted research grants from Gilead unrelated to this work, and honoraria from Gilead, Merck, and AbbVie. HF has received an honorarium from MSD. HM Consultant/advisor for Abbvie and Gilead. Speaker fees from Abbvie, Gilead, MSD and Medivir. MP has served as a speaker and has worked on several research projects unrelated to this study for which her institute received unrestricted grants from Gilead, Roche, MSD and AbbVie.

Word Count: 3919

Contribution of authors

All authors contributed to interpreting the results, writing and editing the paper.

HF undertook modelling supervised by PV, MH NM and drafted the paper.

MH, NM and PV conceived the study with support from all co-authors.

Abstract: 273 words

Abstract:

Background: Prevention of hepatitis C virus (HCV) transmission among people who inject drugs (PWID) is critical to eliminating HCV in Europe. We estimate impact of current and scaled-up HCV treatment with and without scaling-up opioid substitution therapy (OST) and needle and syringe programmes (NSP) across Europe over the next 10 years.

Methods: We collected data on PWID HCV treatment rates, PWID prevalence, HCV prevalence, OST and NSP coverage from 11 European settings. We parameterized a HCV transmission model to setting-specific data that projects chronic HCV prevalence and incidence among PWID.

Results: At baseline, chronic HCV prevalence varied from <25% (Slovenia/Czech Republic) to >55% (Finland/Sweden), and <2% (Amsterdam/Hamburg/Norway/Denmark/Sweden) to 5% (Slovenia/Czech Republic) of chronically infected PWID were treated annually. Current treatment rates using new direct acting antivirals (DAAs) may achieve observable reductions in chronic prevalence (38-63%) in 10 years in Czech Republic, Slovenia and Amsterdam. Doubling HCV-treatment rates will reduce prevalence in other sites (12-24%, Belgium/Denmark/Hamburg/Norway/Scotland) but is unlikely to reduce prevalence in Sweden and Finland. Scaling-up OST and NSP to 80% coverage with current treatment rates using DAAs could achieve observable reductions in HCV prevalence (18-79%) in all sites.

Using DAAs, Slovenia and Amsterdam are projected to reduce incidence to 2 per 100pyrs or less in 10 years. Moderate to substantial increases in current treatment rates are required to achieve the same impact elsewhere, from 1.4-3 times (Czech Republic/France), 5-17 times

(France/Scotland/Hamburg/Norway/Denmark/Belgium/Sweden), to 200 times (Finland). Scaling-up OST and NSP coverage to 80% in all sites reduces treatment scale-up needed by 20-80%.

Conclusions: Scale-up of HCV treatment and other interventions is needed in most settings to minimise HCV transmission among PWID in Europe.

Lay summary: Measuring the amount of HCV in the population of people who inject drugs is uncertain. To reduce HCV infection to minimal levels in Europe will require scale-up of both HCV treatment and other interventions that reduce injecting risk (especially opioid substitution treatment and provision of sterile injecting equipment).

Introduction

Chronic hepatitis C virus (HCV) infection is a leading cause of liver disease and morbidity causing more deaths than HIV in the US and other high income countries [1-4]. Preventing HCV transmission among people who inject drugs (PWID) is critical for averting future liver disease in Europe and elsewhere [5] and new HCV infections in this group[6]. Primary prevention through opioid substitution treatment (OST) and high coverage needle and syringe programmes (NSP) can reduce HCV transmission among PWID [7, 8] and averts new HCV infections,[9] but substantial reductions in HCV prevalence are unlikely to be achieved without scaling up HCV treatment [10-15].

The arrival of highly effective and short duration direct acting antivirals (DAAs) with cure rates (sustained viral response or SVR) above 90% for all genotypes has made HCV "treatment as prevention" more than a theoretical possibility [16-18]. However, the current high cost of DAA regimes (often >€30,000 per treatment regime in higher income countries) is a barrier to scaling up treatment in most countries. European guidelines, that previously recommended prioritising DAAs for patients with advanced liver disease, now suggest HCV treatment should also be provided to people with a risk of transmitting HCV, such as PWID [19, 20]. Although a recent economic model suggested that in general it is more cost-effective to delay treatment of mild disease until more moderate stages of fibrosis[21], when these individuals have on-going transmission risk they should be prioritised for early treatment over other patient groups [22].

In this paper, we estimate the current HCV treatment rates and coverage of OST and NSP in PWID across 11 sites in Europe. We assess the impact of these and scaled-up HCV treatment rates and other primary prevention on HCV prevalence and incidence over the next ten years.

Methods

The model

We used a dynamic deterministic mathematical model of HCV transmission among PWID, stratifying PWID according to intervention status (no OST or NSP, on OST, NSP, or both) alongside HCV infection and treatment status (susceptible never infected, previously infected, chronically infected, on treatment, treatment failure [9, 23]). In three sites (Czech Republic, Finland and Sweden) PWID are also stratified by drug type (opioid or methamphetamine/amphetamine). PWID enter the model through a constant rate that individuals initiate injecting; all PWID are assumed initially susceptible to HCV infection (Figure 1a). Susceptible PWID can become infected at a per-capita rate proportional to the background prevalence of disease which changes as HCV treatment increases. Transmission is reduced by a fixed multiplicative cofactor dependent on OST and NSP status (Figure 1b). Once infected, PWID either transition to the chronically infected group (Ab+, RNA+) or spontaneously clear infection and transition to the previously infected group (Ab+, RNA-). This previously infected group are assumed to be re-infected and clear infection at the same rate as susceptible PWID[24-26]. Chronically infected PWID (both primary and re-infection) can be treated; if treatment is successful and SVR attained, PWID transition to the previously infected group. However, if SVR is not attained PWID transition to the treatment failure group. In the baseline model, treatment failures cannot be retreated (Figure 1a); once treatment is switched to DAAs we assume treatment failures can be retreated. PWID leave the model through permanent cessation of injecting or drug-related or non-drug related mortality. All PWID enter the model with no coverage of OST or NSP, and transition between the different intervention states (OST and/or NSP) at site-specific fixed per-capita

rates (Figure 1b, Tables S1a-S1k). Further details of the model including model equations are in the Supplementary materials.

Model parameterisation and calibration

The model was parameterised to each of the 11 sites (Table 1 and Supplementary Tables S1a-S1l for site specific information).

For sites with opioid injecting only, 2,500 model parameter sets were randomly sampled from the parameter uncertainty distributions (see Tables S1a-S1l). For each parameter set, the model was fit to the PWID population size by varying the rate that individuals initiate injecting, to OST and NSP coverage levels by varying the recruitment rates onto OST and NSP, and to either the chronic or antibody HCV prevalence at a site-specific time-point by varying the transmission rate. For Czech Republic, Finland and Sweden the model was fit to more parameters - see Supplementary Materials for further details. HCV incidence was estimated from model inputs assuming a stable epidemic except for Amsterdam where additional data were available suggesting a decreasing PWID population size and declining incidence[15].

In sites with opioid and meth/amphetamine injecting, we assume that baseline risk of HCV transmission is the same for all PWID [27-29], there is equal NSP coverage across both types of injectors, but only opioid users can be recruited on to OST.

In all but four sites (Czech Republic, Finland, Sweden and Norway), HCV treatment of PWID was modelled only amongst those on OST for initial analyses as in these sites only PWID on OST are currently treated.

Model projections and analyses

Data on PWID treatment numbers for each site were scaled to give a rate per 1000 PWID as well as percentage of chronic HCV infections treated in 2015/16. By scaling to give a rate based on total PWID population size we can easily compare current and projected future treatment numbers between all sites. All known increases in treatment prior to 2015 were included in the model.

We used the model to project the change in prevalence and incidence between 2016 and 2026 if treatment is switched from IFN-based therapies to new DAAs (SVR rate 90% (85-95%) and current treatment rates per 1000 PWID are either maintained, doubled, or increased to 50 per 1000 PWID treated annually. Impact projections either assumed current coverages of OST and NSP are maintained or OST and NSP are scaled-up to 80% coverage (if not already achieved). We determined the annual treatment number (expressed as a rate of treatment per 1000 PWID) needed to reduce incidence to 2 per 100 person years (2%) by 2026. This is the number of treatments annually per 1000 PWID and is therefore constant when projecting to 2026.

We estimated the z-score associated with the mean difference in chronic prevalence given the uncertainty in chronic HCV generated by the model. We categorised a z-score less than 0.5 as a modest change (unlikely to be observed), between 0.5-1.5 as a moderate change (may be observable), and scores greater than 1.5 or 3.0 as changes that are increasingly and highly likely to be observed.

Uncertainty analysis

To consider the effect of uncertainty within the underlying parameters, we performed a linear regression analysis of covariance on the relative decrease in HCV prevalence and incidence between 2016 and 2026 when current treatment rates are doubled. For each site, the proportion of each model outcome's sum-of-squares contributed by each parameter was calculated to estimate the importance of each parameter to the uncertainty[30].

Results

Baseline HCV Treatment Rates

HCV treatment of PWID started at different times across the sites, ranging from 1997 (Slovenia) to 2009 (Norway) with very few PWID having been treated in Finland. Figure 2 shows the percentage of chronic HCV prevalent cases among PWID that were treated in 2015/16 based on data from each site – varying from <0.1% in Finland, to 0.5-2% in Sweden, Denmark, Belgium, Norway and Amsterdam, and >5% in Czech Republic and Slovenia.

Model projections

(a) Chronic HCV prevalence among PWID

At baseline in 2016, projected chronic prevalence varied from <25% in Czech Republic (21% (95% CrI 18-24%)) and Slovenia (16% (11-22%)), to >55% in Finland (56% (53-59%)) and Sweden (60% (57-63%)). Figure 3 shows projected baseline and 10 year chronic HCV prevalence among PWID in each setting for different levels of scale-up of HCV treatment with new DAAs. Figure 4 shows the same projections but with scale-up in OST and NSP coverage to 80%.

(i) Switching to DAAs, treatment rate maintained

In the majority (8/11) of the sites the difference in projected chronic HCV prevalence after 10 years if current treatment rates with DAAs remain constant is <5%. In these sites the median absolute difference ranges from <1.5% in Finland, Sweden and Belgium up to 3-4% in Norway, Denmark, France, Hamburg, and Scotland. This difference is substantially smaller than the uncertainty in the baseline chronic HCV prevalence in the sites. This equates to a relative decrease of <10% at each site (see Supplementary Materials).

In the remaining three sites (Amsterdam, Czech Republic and Slovenia), there is a much greater relative decrease in chronic HCV prevalence between 2016 and 2026 from switching to DAAs; 37.5% (26.6-51.8%) in Czech Republic and 49.3% (25.0-98.0%) in Slovenia. In Amsterdam, the decreasing population size and concurrent decrease in transmission contribute around 90% of the relative decrease of 51.8% (28.7-65.7%) in chronic prevalence between 2016 and 2026. These sites have a z-score >3.0 indicating that an observable change in chronic prevalence will likely occur by switching to DAAs with current treatment rates.

If all sites switched to DAAs with current treatment rates and concurrently increased OST and NSP coverage to 80%, the model projects a reduction in prevalence in all sites, from less than 20% in Finland (17.6 (10.0-27.9%)) and Hamburg (19.5% (11.7-27.6%)), 30-50% in Scotland, Sweden, France, Norway, Denmark and Belgium, to >50% in Czech Republic and Amsterdam, and >75% in Slovenia. The differential benefit of scaling-up OST and NSP alongside treatment on reducing chronic HCV prevalence ranges from greater than 10 to less than 1.5 times because of baseline coverage. For example, in Finland, Sweden and Belgium scaling-up OST and NSP with current HCV treatment rates reduces chronic HCV prevalence in 10 years by 17.1%, 31.1% and 48.4% respectively, compared to 0.1%, 1.8% and 4.4% reduction without OST and NSP scale-up. In contrast, there is only a small projected

improvement in Amsterdam and Czech Republic which already have high coverage of OST and NSP (Supplementary Materials Tables S1a-S1k); other sites are projected to improve reductions in chronic HCV prevalence from 2-3 times (Slovenia, Hamburg and Scotland) and 5-6 times in France, Denmark and Norway (Supplementary Materials Table S2).

(ii) Switching to DAAs, treatment rate doubled

For sites with high baseline chronic prevalence (>55% at baseline) and low treatment rates (<1% of chronic infections treated at baseline), for example Sweden and Finland, doubling DAA treatment rates has little effect on the projected prevalence in 2026 (0.4% (0.3-0.6%) and 5.2% (3.3-10.4%) relative decrease respectively) if OST and NSP are maintained at current coverage. For sites with moderate chronic prevalence (30-50% at baseline) and <2.5% of chronic infections being treated annually in 2015/16 (Belgium, Denmark, Hamburg, Norway, Scotland), doubling DAA treatment rates could reduce chronic HCV prevalence from 11.6% relative decrease (Belgium) up to 23.5% (Scotland).

France has a moderate chronic prevalence (47.3%) at baseline and high initial treatment rate (4.5% (2.4-8.3%) of all chronic infections treated annually). When their treatment rate is doubled with DAAs this yields a greater relative decrease in chronic prevalence than other sites with moderate prevalence (36.4% (16.7-85.5%)). The credibility intervals are wide because of uncertainty in the estimates of HCV treatment rates.

In Czech Republic and Slovenia, doubling DAA treatment rates is projected to reduce chronic prevalence by >90% (Figure 3), and in Amsterdam by 55.8% (32.8-69.6%).

Increasing OST and NSP to 80% coverage and doubling DAA treatment rates is projected to reduce chronic prevalence between 17.9% (10.3-28.2%) in Finland to 99.5% (91.8%-99.9%) in Slovenia. In sites with high baseline treatment rates (Czech Republic and Slovenia), the decrease in prevalence is primarily due to doubling treatment rates (97.3% and 91.6% decrease in Czech Republic with and without scaled-up OST and NSP, respectively, and 99.5% and 97.4% in Slovenia). For sites with low baseline treatment rates and low coverage of OST and NSP, it is the increase in OST and NSP that drives the decrease in chronic prevalence rather than the doubling in treatment rates – in Finland the decrease changes from 0.4% to 17.9% when additionally scaling-up OST and NSP, from 5.2% to 35.5% in Sweden and from 11.6% to 55.6% in Belgium.

(iii) DAA treatment rate 50 per 1000 PWID

Increasing annual DAA treatment rates to 50 per 1000 PWID with current OST and NSP coverage leads to substantial reductions in chronic HCV in all sites (Figure 3). In the high prevalence sites of Finland and Sweden chronic prevalence reduces by about half by 2026. Conversely, in most moderate prevalence sites (Belgium, Hamburg, Scotland, Norway and Denmark) chronic HCV prevalence decreases by 70% or more, although in France the decrease is smaller and more uncertain (47.6% (21.7-73.8%)). In low prevalence settings (Czech Republic and Slovenia), chronic prevalence is projected to decrease by around 99% by 2026.

In projections with OST/NSP scale-up to 80%, prevalence decreases by more than three-quarters in all sites, with 7/11 sites (Scotland, Denmark, Norway, Belgium, Amsterdam, Czech Republic and Slovenia) projecting a decrease of >95%.

(b) HCV Incidence among PWID

Baseline projections of incidence before 2015 agree with observed incidence estimates where data were available (Supplementary Materials). Projected changes in incidence from 2016 to 2026 are shown in Supplementary Figures 2 and 3, without and with scale-up of OST and NSP to 80% coverage using DAAs. HCV incidence is projected to remain largely unchanged with current OST and NSP coverage in all but 3 sites if current HCV treatment rates are maintained using DAAs, however if OST and NSP are scaled-up to 80% coverage, projections estimate a relative decrease in incidence of over 35% at all sites.

Figure 5 shows the treatment number per 1000 PWID required in 2016/17 to reduce incidence to 2 per 100 pyrs (2%) among PWID by 2026 with and without scale-up of OST and NSP to 80% coverage. In Amsterdam, an incidence of 2% (1-3%) was already estimated in 2016, and so just switching to DAAs ensured an incidence <2% by 2026 in 99% of model runs. In Slovenia, just switching to the new DAAs and maintaining current treatment rates is likely to decrease incidence to <2% by 2026 (projected by 78% of model fits), with an increase in treatments rates by 20% being needed to ensure this impact in the other 22% of model fits. In Czech Republic switching to DAAs would achieve 2% incidence in <10% of model fits, and increasing current treatment rates by 43% over all model runs would ensure the decrease. In all other sites a substantial increase in HCV treatment rates (in the absence of any increase in OST and NSP coverage) is needed to reduce HCV incidence to 2%, ranging from 3 to 5 times the current treatment rates in France and Scotland, to between 6-9 times in Hamburg, Norway, Denmark, Belgium, 17 times in Sweden, and 200 times in Finland. If OST and NSP are scaled-up to 80% coverage, maintaining current treatment rates is sufficient to achieve an incidence of 2% in 2026 in Amsterdam and Slovenia (100% of model fits), may achieve this impact in Belgium, Czech Republic (84% and 50% of model fits), but

is unlikely to (<10% of model fits) in other settings. Alongside increased OST and NSP, France, Denmark, Norway, Scotland, Hamburg, Sweden and Finland would need to scale-up their baseline treatment rates by 2.2, 2.8, 2.8, 3.6, 4.7, 10.3 and 159-fold, respectively. This is 20-60% less than if OST and NSP had not been scaled-up.

(c) Uncertainty analysis

The sensitivity analysis indicates that for most sites, uncertainty in three main factors contribute to variation in the relative decrease in chronic prevalence and incidence between 2016 and 2026 when treatment rates are doubled, but with differing levels of influence between the sites (Supplementary Materials Figure S4). The PWID population size contributes 34-63% of the variation in Finland, Belgium, Scotland, Slovenia and Norway, and 80% in Sweden, whilst the prevalence estimates contribute 32-53% of the variation in five of the sites (Slovenia, Belgium, Czech Republic, Denmark and Hamburg). The duration of injecting is most important in Amsterdam, contributing 85% of the variation, but also contributes 25-48% in Scotland, Hamburg, Denmark, Norway, Belgium and Finland. In France, the estimated treatment rate contributes 80% of the variation.

Discussion

Main Findings

Treatment scale-up is needed to achieve observable reductions in chronic HCV prevalence among PWID in most sites in Europe , even with new DAAs. Doubling DAA treatment rates may lead to observable reductions (12-24% decrease) in chronic prevalence by 2026 in Belgium, Denmark, Hamburg, Norway and Scotland; but not in Finland or Sweden. Exceptions include Czech Republic, Slovenia, and Amsterdam, which at current HCV treatment rates are projected to reduce chronic HCV prevalence from a third to a half by

2026. This is due to the low or decreasing prevalence of infection in these settings. Alternatively, increasing OST and NSP coverage to 80% with current HCV treatment rates would reduce chronic HCV prevalence by 17-20% in Finland and Hamburg and 30-79% in all other sites. Reducing HCV incidence to less than 2% by 2026 requires little action in Amsterdam, Czech Republic and Slovenia, whereas in Belgium, Denmark, Hamburg, Norward and Scotland it will require at least a 5-fold increase in current HCV treatment rates, or 1.8-4.7-fold if OST and NSP are scaled up to 80% coverage.

Strengths and Limitations

Our model projections and their interpretation are influenced strongly by uncertainty in the parameters and evidence base. First, we collected information from a range of sources and obtained data not routinely collected across Europe (e.g. number of PWID treated for HCV) [6, 31]. Unfortunately, data collection was inconsistent across sites, particularly estimates of PWID population size which were used to estimate HCV treatment rates. Reliable PWID population size estimates are difficult to obtain and except for Amsterdam where evidence suggests a falling population [15, 32], we had to assume stable populations.

Second, uncertainty in the chronic HCV prevalence among PWID contributed substantially to the uncertainty in our projections, with estimates generated from a diverse range of sources and rarely (except for Scotland) from ongoing community based surveillance [6, 33]. Third, the duration of injecting drug use is difficult to estimate precisely and contributed to model uncertainty. We sampled the average injecting duration from a range extending from 6 to over 20 years, and in the absence of clear evidence assumed that opioid and methamphetamine injectors had similar durations. If the true duration is towards the higher end of our ranges, scaling-up HCV treatment will have greater impact on transmission, and if

towards the lower end, scaling-up OST and NSP will have a greater contribution on reducing transmission [34].

Fourth, DAA SVRs for PWID in "real world" settings are yet to emerge, and so we assumed a range of 85-95%[35, 36]. Given the short treatment duration and early treatment of predominantly mild disease, it is likely that SVRs will be very high, although it is possible that as treatment is scaled-up among more vulnerable PWID this SVR may reduce. In general, the impact of HCV treatment in our projections is relatively robust to variations in SVR, although uncertainty in SVR becomes more influential in settings with lower chronic prevalence and higher HCV treatment rates. Furthermore, we assumed that PWID who had either cleared HCV spontaneously or after successful treatment had the same risk of re-infection as the susceptible population of PWID i.e. the per capita transmission probability of re-infection was the same as for primary infection. There is some evidence to suggest that previous spontaneous clearance could result in higher rates of clearance for subsequent re-infection[24], but similar data surrounding spontaneous clearance of re-infections after SVR does not exist, and infrequent testing intervals can contribute bias as some re-infections may go unnoticed[24, 37]. Observational studies have reported that re-infection after SVR can be of a similar, higher or lower rate than the background rate of infection[38-42], indicating uncertainty in the evidence. However, if re-infection risk was lower than primary infection for people achieving SVR, or spontaneous clearance higher for re-infections, then our model projections represent conservative estimates for the number of treatments needed to reduce prevalence and incidence across the different sites.

Fifth, we recorded substantial differences in coverage of OST and NSP between sites which are incorporated into the baseline model. In subsequent intervention scenarios, we either considered no scale-up of these interventions, or assumed their scale-up to 80% coverage. This optimistic scenario may over-estimate the likely impact of what could be achieved from

scaling-up OST and NSP, although some of our sites demonstrate such coverage is possible. However, even if this scale-up is possible, it is unlikely that it would be achieved quickly, so these projections may over-estimate the real reduction in HCV that could be achieved from scaling-up OST and NSP. Sixth, the model does not incorporate information on HCV case-finding and any future difficulty in diagnosing and treating PWID with chronic HCV when HCV transmission and prevalence have fallen to low levels, but this limitation will only affect a small number of the most optimistic model projections.

Seventh, we have not modelled HIV co-infection which varies across Europe and may impact both on linkage to services and morbidity outcomes. Finally, we assume no change in injecting risk behaviour following HCV treatment – apart from through exposure to OST and NSP which is also included prior to HCV treatment. If injecting risk was reduced following treatment [43], our assumption provides conservative projections of impact.

Implications and Comparisons with Other Literature

Multiple studies in specific countries and across Europe have used statistical and mathematical model projections to suggest that new DAA treatments need to increase in order to reverse trends in End Stage Liver Disease [44-48]. However, to project impact on HCV transmission, a dynamic transmission model that can track both re-infection and prevention of future infections is required, alongside information on the number and proportion of individuals from key populations like PWID treated for HCV infection. Consequently, there are fewer analyses that project impact on HCV transmission.

An earlier study revealed a 2-3 fold difference in chronic HCV prevalence and 4-5 fold difference in baseline HCV treatment rates in seven cities in the UK [49]. We also found

considerable heterogeneity between sites in Europe. For example, Czech Republic and Slovenia both have baseline chronic prevalence of less than 30% [28, 50, 51], whilst in Finland and Sweden it is over 55%. Treatment rates also varied 2-3 fold. At baseline, 8/11 sites had low treatment rates (<10/1000 PWID treated annually), whereas France had a much higher treatment rate (21/1000 PWID treated annually), a consequence of the high access to HCV treatment in France compared to other countries[52]. Our results also show a greater decrease in prevalence for Amsterdam than other studies have projected [15, 53], however this could be due to differences in modelling the decreasing epidemic to achieve the incidence estimate, and differences modelling the PWID population and transmission dynamics.

The lack of ongoing surveillance data, including PWID prevalence and HCV treatment rates amongst PWID, in many European settings and comparable indicators between countries is important and a public health concern. Our model projections show that scaling-up OST and NSP combined with switching to DAAs with comparatively small increases in the number of PWID treated could generate substantial observable reductions in HCV prevalence in several sites. However, robust HCV surveillance data among PWID were not always available and chronic HCV prevalence was uncertain. To ensure that empirical evidence of the impact of HCV treatment as prevention can be generated, it is important that more attention is given to establishing robust surveillance systems to reduce the uncertainty surrounding chronic HCV prevalence among PWID. The potential and relative costs of introducing effective HCV surveillance are trivial compared to the costs of HCV treatment – and need to be encouraged across Europe.

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Tables

Table 1: Parameter table

Key parameters used in the modelling for each of the sites. PWID population size and prevalence estimates shows mean (95% CI) unless otherwise stated. Mortality rates are given per year. The range for the number of PWID treated per 1000 PWID is estimated using the number of treatments in each site and the PWID population size. References are given in Tables S1a-S1k in Supplementary Material.

Parameter	Value	Notes
PWID population size:		All sampled from a normal distribution
Amsterdam	2621 (1946-3374) in 2009 1874 (1341-2455) in 2014	
Belgium	9080 (6356 – 11804)	
Czech Republic	41816 – 46563	Range – no point estimate available
Denmark	16500 (13000 – 19000)	
Finland	15611 (13770 – 22655)	
France	80000 (65000 – 95000)	
Hamburg	8492 (7582 – 9436)	
Norway	15500 (10500 – 20150)	
Scotland	16000 (11500 – 19400)	
Slovenia	6000 (4200 – 7800)	
Sweden	8021 – 26550	Maximum and minimum PWID population size estimates.
PWID mortality rate:		All sampled from a Poisson distribution
Amsterdam	2.4% per year	
Belgium	2.5% per year	
Czech Republic	0.8% per year	

Denmark	2.0% per year		
Finland	2.0% per year		
France	1.3% per year		
Hamburg	0.7% per year		
Norway	1.9% per year		
Scotland	1.0% per year		
Slovenia	0.7% per year		
Sweden	2.0% per year		
HCV antibody prevalence among PWID and year prevalence fit to			All sampled from a normal distribution. In all cases HCV antibody prevalence is adjusted to chronic prevalence by assuming a 26% (22-29%) spontaneous clearance rate [54]
Amsterdam	59.4% (54.8 – 64.0%)	2007	
Belgium	43.3% (34.3 – 52.4%)	2012	
Czech Republic	35.0% (31.6 – 38.5%)	2005	
Finland	76.0% (72.4-79.4%)	2014	
France	66.4% (60.3–71.9%)	2011	
Hamburg	67.7% (62.3-72.8%)	2014	
Scotland	58.0% (55.8 – 60.2%)	2013/14	
Slovenia	27.3% (19.1 – 35.5%)	mid-2010	
Sweden	81.7% (79.6 – 83.6%)	2014	
HCV chronic prevalence among PWID			
Denmark	35.0 – 45.0%	2014	
Norway	45% (42.6 – 47.5%)	2007	
Number PWID treated per year:			1. Only those on OST are initially eligible for treatment. 2. All PWID can be treated.
	Total treated in each site per year	Number treated per 1000 PWID per year	
Amsterdam	2005-2016: 15	2005-2016: 6.1 – 11.2	1.
Belgium	2004-2016: 30	2004-2016: 5.7 – 10.6	1.
Czech Republic	2002-2011: 370	2002-2011: 7.9 – 8.8	

	2011-2016: 540	2011-2016: 11.6 – 12.9	2.
Denmark	2002-2014: 53 2014-2015: 50 2014-2016: 100	2002-2014: 2.8 – 4.1 2014-2015:2.6-3.8 2014-2016: 5.3-7.7	1.
Finland	2006-2016: 5	2006-2016: 0.06	1.
France	2001-2016: 1705 (923 – 3148)	2001-2016:10.5 – 43.3	1. Note: these are the calculated number treated based on the treatment rate for people who have injected at least one in the last year.
Hamburg	2005-2011: 60 2011-2016: 72	2005-2011: 6.2 – 7.9 2011-2016: 7.6 – 9.5	1.
Norway	2009-2016: 100	2009-2016: 5.0 – 9.5	70% treatment are amongst those on OST and 30% treatment amongst those not on OST.
Scotland	2005-2008: 60 2008-2009: 90 2009-2016: 150	2005-2008: 3.1 – 5.2 2008-2009: 4.6-7.8 2009-2016: 7.7-13.0	1.
Slovenia	1997-1999: 2 1999-2008: 5 2008-2016: 62	1997-1999: 0.3 – 0.5 1999-2008: 0.6 – 1.2 2008-2016: 7.9 – 14.8	2.
Sweden	1997-2016: 90	1997-2016: 3.4 – 11.2	2.

Figure legends

Figure 1: Schematics of HCV transmission (1a) and OST and NSP interventions (1b) in the model

Figure 1a: Infection component of the model

Figure 1b: OST and NSP intervention component of the model

Figure 2: Percentage of estimated PWID with chronic HCV infections treated annually at baseline (2015/16) for each site. Bars indicate the median and interquartile range and whiskers show the 95% credibility intervals.

Figure 3: Baseline and projected 10 year chronic HCV prevalence among PWID in multiple sites in Europe for various treatment intervention scenarios. Baseline chronic prevalence (blue boxes) and projected 10 year chronic prevalence if either current treatment rates continue with new DAAs (green boxes), treatment rates are doubled with new DAAs (yellow boxes), or increased to 50 per 1000 PWID annually with new DAAs (pink boxes). Bars indicate the median and interquartile range and whiskers show the 95% credibility intervals.

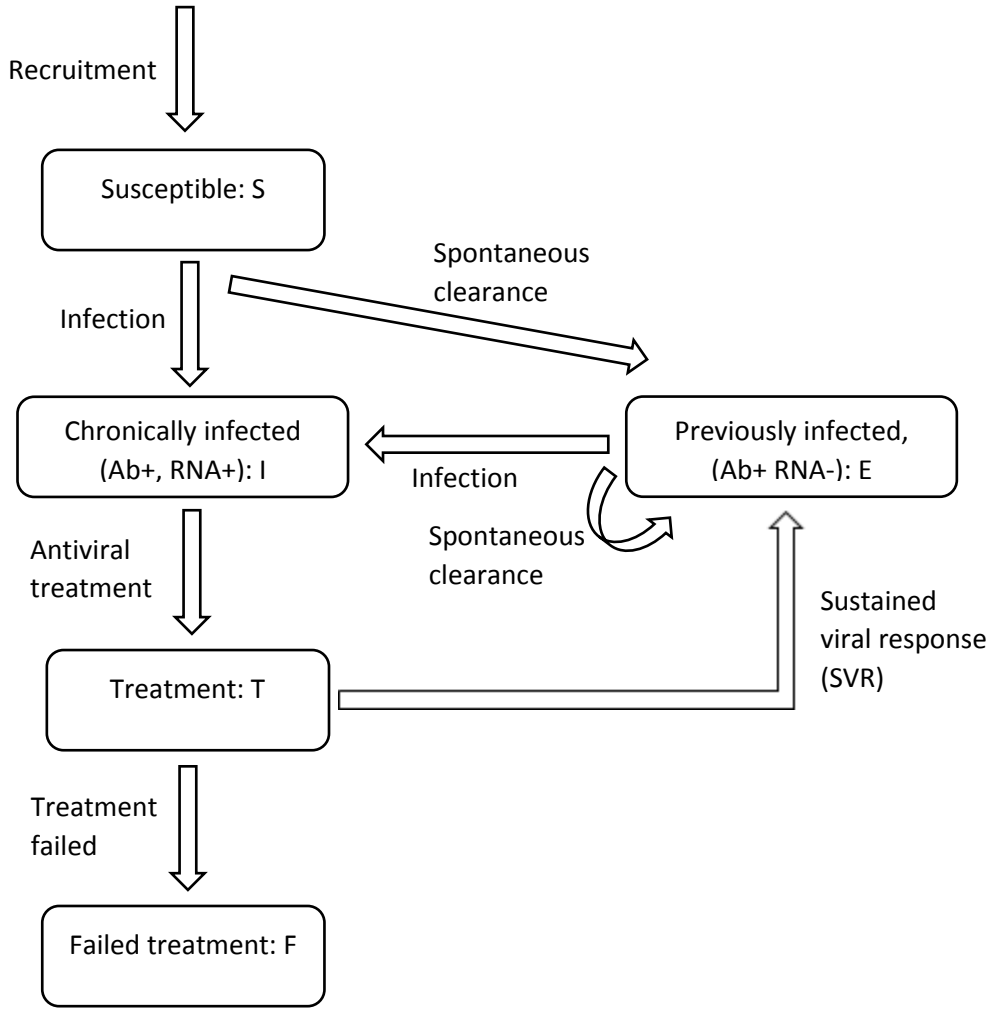
Figure 4: Baseline and projected 10 year chronic HCV prevalence among PWID in multiple sites in Europe for various treatment intervention scenarios with OST and

NSP scaled-up to 80% coverage. Baseline chronic prevalence (blue boxes) and projected 10-year chronic prevalence if either current treatment rates continue with new DAAs (green boxes), treatment rates are doubled with new DAAs (yellow boxes), or increased to 50 per 1000 PWID annually with new DAAs (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.

Figure 5: Current and projected number of treatments per 1000 PWID to reduce incidence to 2 per 100 pyrs by 2026. Current number of treatments per 1000 PWID at baseline (2015/16, blue) and required scale-up in number of treatments per 1000 PWID initially needed per year (2016/17) if current OST and NSP coverage is maintained (green, median and 95% credibility interval shown in figure) or if OST and NSP are scaled to 80% coverage (yellow) to reduce incidence to 2 per 100 pyrs (2%) by 2026. Based on data from the sites we have: [1]Treatment initially given only to those on OST. [2]Treatment initially given to all PWID. [3]70% treatment to PWIDs on OST, 30% treatment to PWIDs not on OST.

Figures

1a and 1b



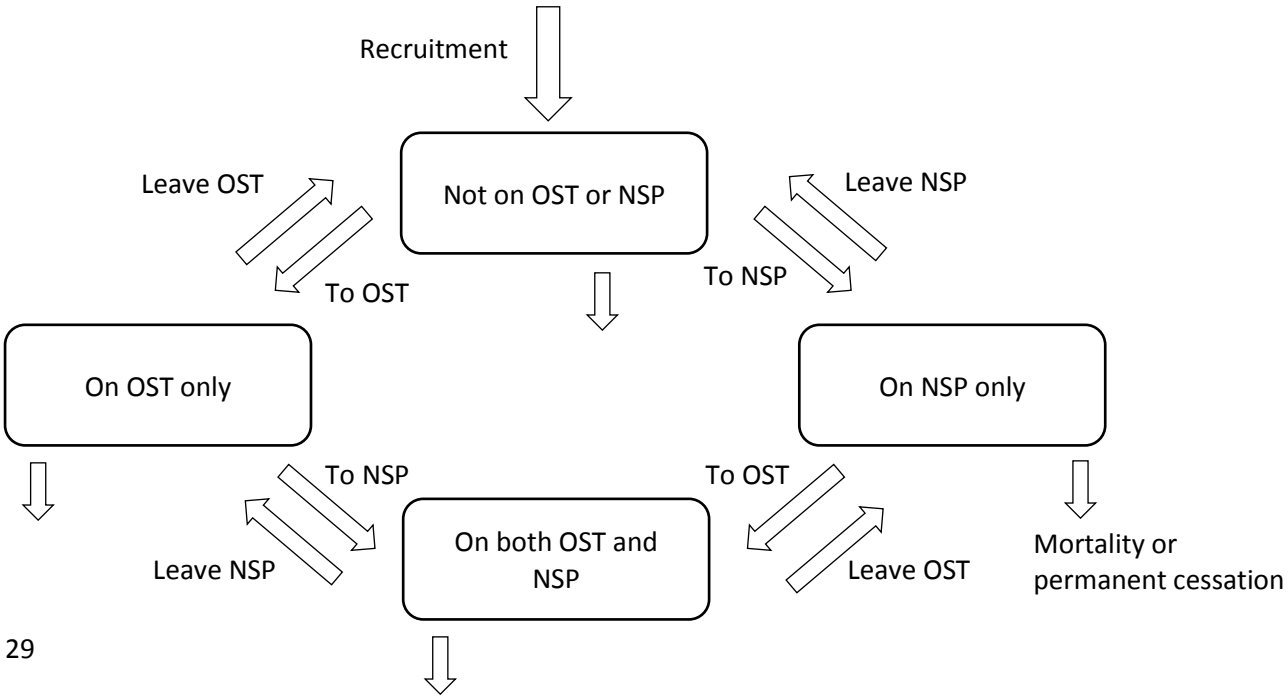


Figure 2

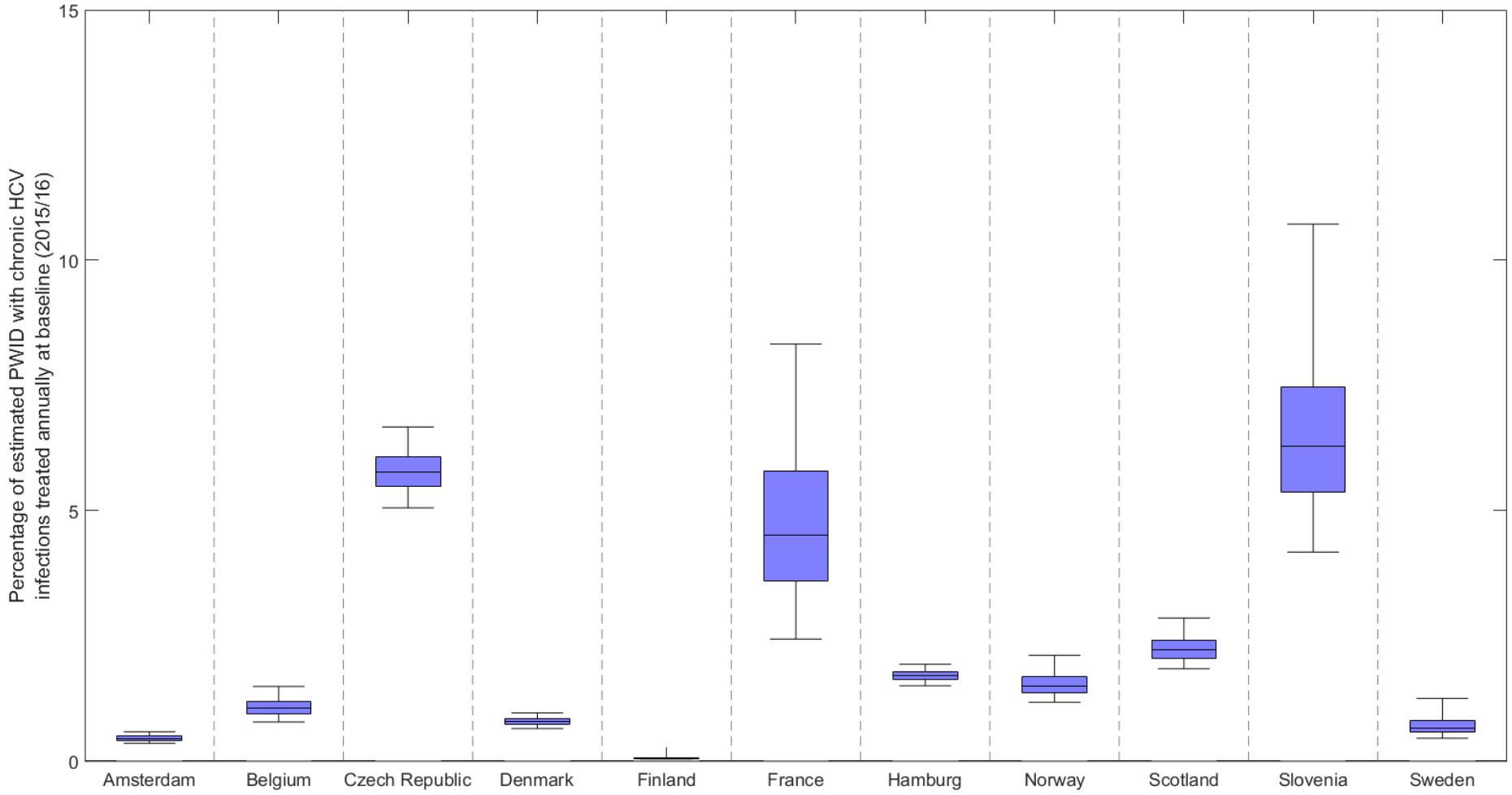

Percentage of estimated PWID with chronic HCV infections treated annually at baseline (2015/16)
15
10
5
0
Amsterdam
Belgium
Czech Republic
Denmark
Finland
France
Hamburg
Norway
Scotland
Slovenia
Sweden

Figure 3

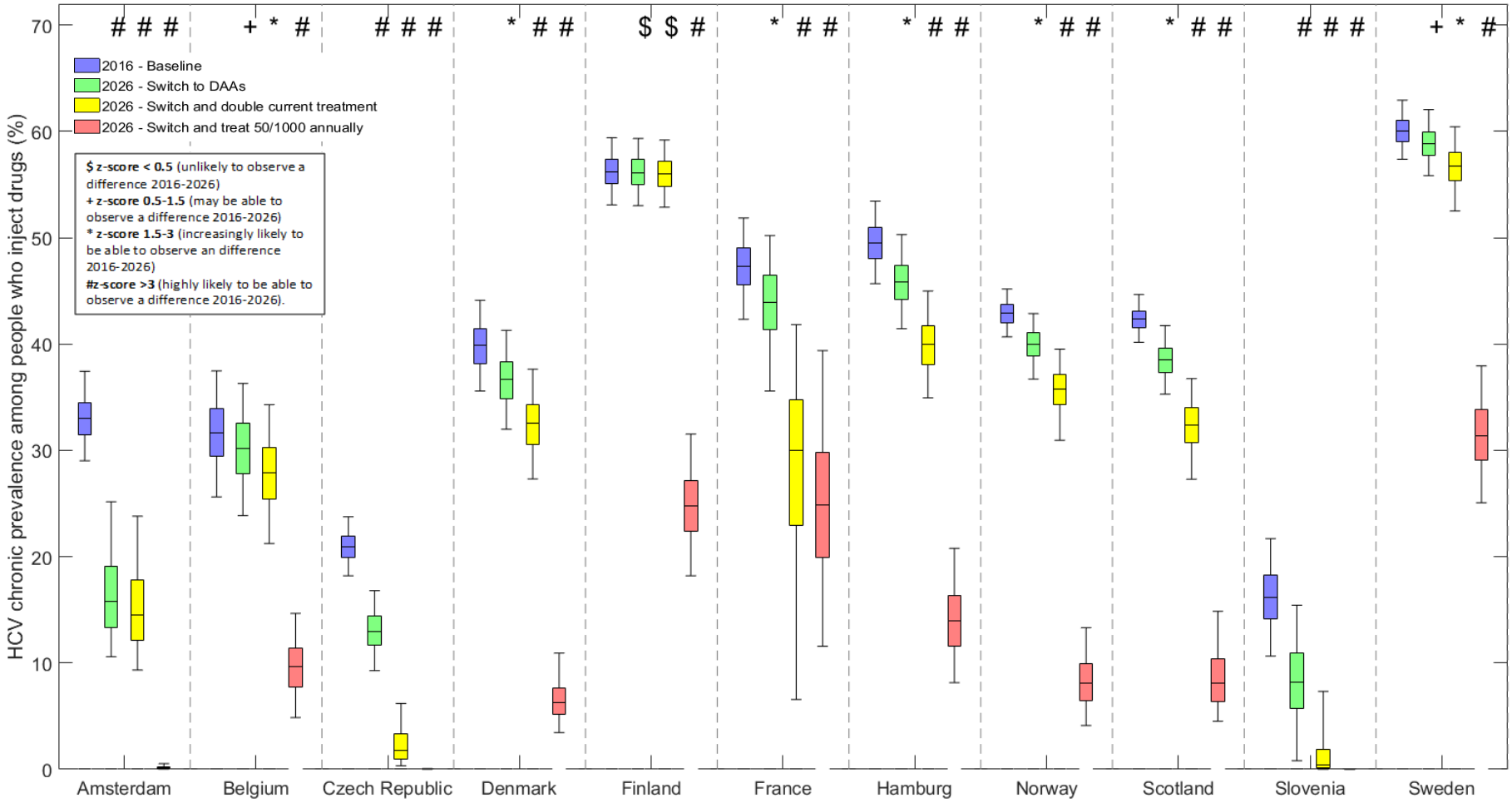

HCV chronic prevalence among people who inject drugs (%)
0
10
20
30
40
50
60
70
2016 - Baseline
2026 - Switch to DAAs
2026 - Switch and double current treatment
2026 - Switch and treat 50/1000 annually
$ z-score < 0.5 (unlikely to observe a difference 2016-2026)
+ z-score 0.5-1.5 (may be able to observe a difference 2016-2026)
* z-score 1.5-3 (increasingly likely to be able to observe an difference 2016-2026)
#z-score >3 (highly likely to be able to observe a difference 2016-2026).
# # #
+ * #
# # #
* # #
$ $ #
* # #
* # #
* # #
* # #
# # #
+ * #
Amsterdam
Belgium
Czech Republic
Denmark
Finland
France
Hamburg
Norway
Scotland
Slovenia
Sweden

Figure 4

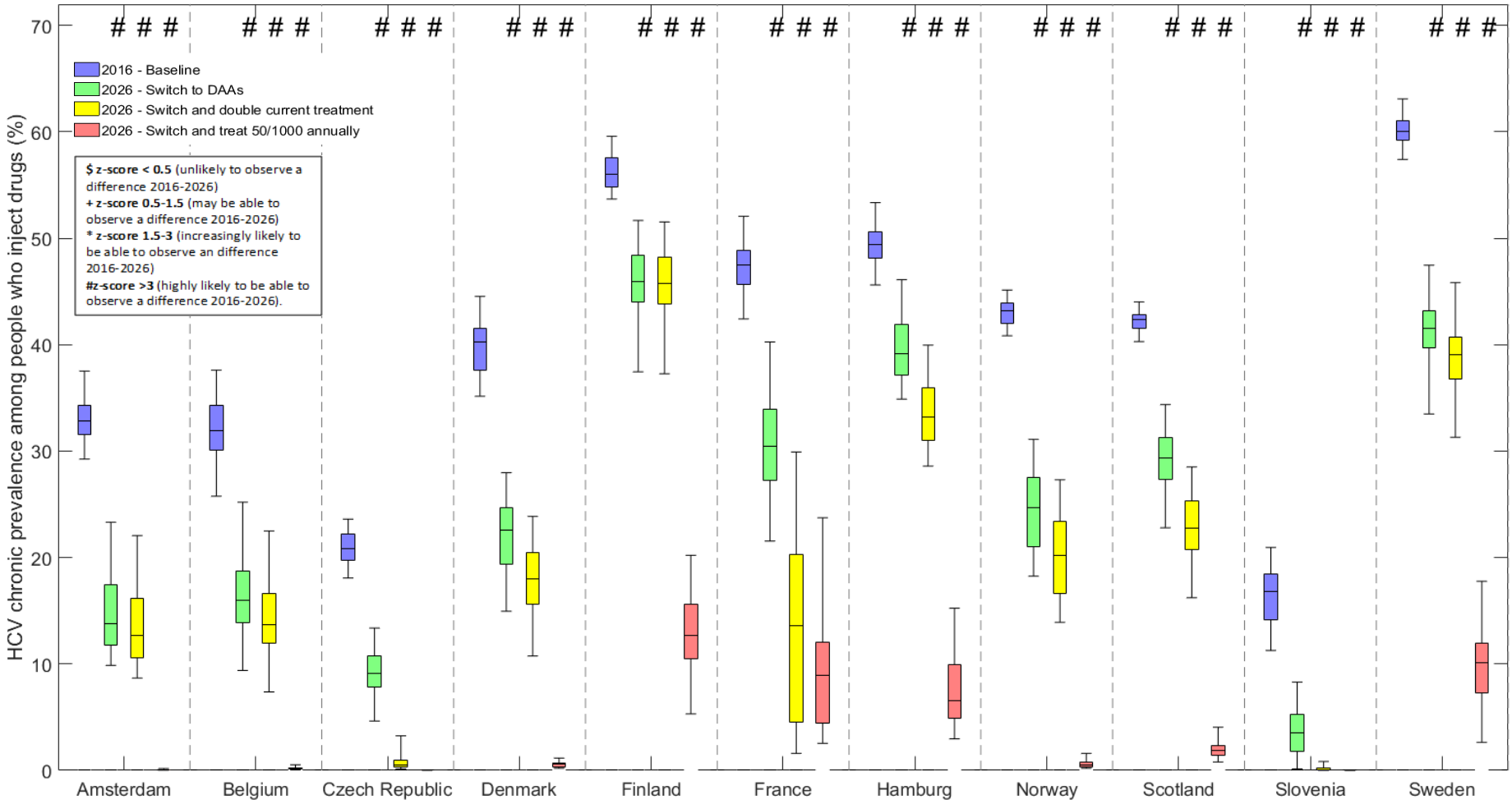
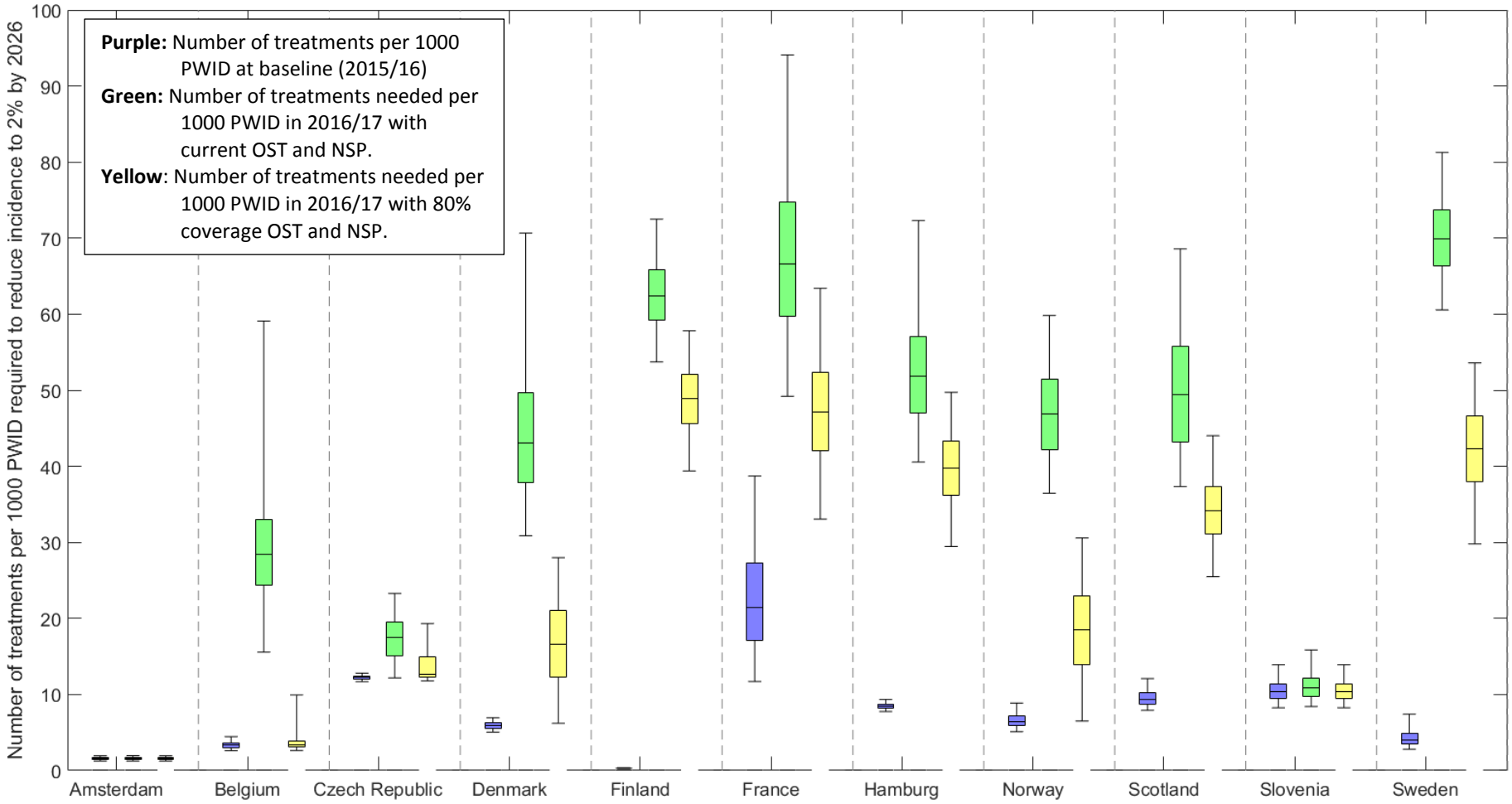

HCV chronic prevalence among people who inject drugs (%)
0
10
20
30
40
50
60
70
2016 - Baseline
2026 - Switch to DAAs
2026 - Switch and double current treatment
2026 - Switch and treat 50/1000 annually
$ z-score < 0.5 (unlikely to observe a difference 2016-2026)
+ z-score 0.5-1.5 (may be able to observe a difference 2016-2026)
* z-score 1.5-3 (increasingly likely to be able to observe an difference 2016-2026)
#z-score >3 (highly likely to be able to observe a difference 2016-2026).
Amsterdam
Belgium
Czech Republic
Denmark
Finland
France
Hamburg
Norway
Scotland
Slovenia
Sweden

Figure 5


Purple: Number of treatments per 1000 PWID at baseline (2015/16)
Green: Number of treatments needed per 1000 PWID in 2016/17 with current OST and NSP.
Yellow: Number of treatments needed per 1000 PWID in 2016/17 with 80% coverage OST and NSP.
Number of treatments per 1000 PWID required to reduce incidence to 2% by 2026
0
10
20
30
40
50
60
70
80
90
100
Amsterdam
Belgium
Czech Republic
Denmark
Finland
France
Hamburg
Norway
Scotland
Slovenia
Sweden