Modelling the potential prevention benefits of a treat-all hepatitis C treatment strategy at global, regional, and country levels: a modelling study

Short title: Transmission prevention of HCV treatment

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Abbreviations:

aOR – adjusted odds ratio

CI – confidence interval

DAA – direct acting antiviral

HCV – hepatitis C virus

HIV – human immunodeficiency virus

IA – infections averted

IDU – injecting drug use

IQR – interquartile range

LMIC – lower and middle-income countries

NSP – needle and syringe provision

OR – odds ratio

OST – opiate substitution therapy

PWID – people who inject drugs

UN – United Nations

WHO – World Health Organization

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Abstract (249/250)

Background: The World Health Organization (WHO) recently produced guidelines advising a treat-all policy for HCV to encourage widespread treatment scale-up for achieving HCV elimination. We modelled the prevention impact achieved (HCV infections averted [IA]) from initiating this policy compared with treating different subgroups at country, regional, and global-levels. We assessed what country-level factors affect impact.

Methods: A dynamic, deterministic HCV transmission model was calibrated to data from global systematic reviews and UN datasets to simulate country-level HCV epidemics with ongoing levels of treatment. For each country, the model projected the prevention impact (in HCV IA per treatment undertaken) of initiating four treatment strategies; either selected randomly (treat-all) or targeted among people who inject drugs (PWID), people aged ≥35, or those with cirrhosis. The IA was assessed over 20-years. Linear regression ~~was used to identify~~identified associations between IA per treatment and demographic factors.

Results: Eighty-eight countries (85% of the global population) were modelled. Globally, the model estimated 0.35 (95% credibility interval [95%CrI]: 0.16-0.61) IA over 20-years for every randomly allocated treatment, 0.30 (95%CrI: 0.12-0.53) from treating those aged ≥35, and 0.28 (95%CrI: 0.12-0.49) for those with cirrhosis. Globally, treating PWID achieved 1.27 (95%CrI: 0.68-2.04) IA per treatment. The IA per randomly allocated treatment was positively associated with a country's population growth-rate, and negatively associated with higher HCV prevalence among PWID.

Conclusions: Appreciable prevention benefits could be achieved from WHO's treat-all strategy, although greater benefits per treatment can be achieved through targeting PWID. Higher impact will be achieved in countries with high population growth.

Keywords: HCV, infections, averted, treat, DAA

Introduction

Hepatitis C virus (HCV) is a bloodborne infection(1). Globally, over 70 million people are infected with HCV(2). An estimated 400,000 people die annually due to HCV-related disease(1, 3, 4).

Direct-acting antiviral (DAA) treatments have made HCV an easily curable infection(5). In 2016, the World Health Organization (WHO) published a Global Health Sector Strategy for eliminating HCV as a public health threat by 2030(6), setting targets to reduce the incidence of new infections by 80%, and HCV-related mortality by 65%. Meeting these targets requires governments to efficiently allocate resources for treating HCV infections, especially where DAA prices are high or resources are low(7).

Historically the emphasis has been on treating people with advanced liver disease(8). However, a wider allocation of treatment is required to eliminate HCV. To encourage widespread treatment scale-up, WHO produced guidelines in 2018 advising that countries should allow access to HCV treatment for all infected individuals: a "treat-all" strategy(9). This HCV treatment strategy will produce clinical benefits, such as reducing the risks of severe liver disease(10), and should also prevent new infections from occurring through treating individuals with ongoing transmission risk(11). Previous analyses have considered who should be treated to achieve greatest morbidity and mortality benefits(12-14), whilst other analyses have considered the cost-effectiveness of different treatment strategies(13). However, these analyses have generally not included prevention benefits unless they focussed on people who inject drugs (PWID), assuming these benefits would be negligible when not treating such high-risk groups(15). To help countries understand the overall benefits of WHO's new treat-all policy, it is important to evaluate its prevention benefits and determine how country-level demographic and epidemiological differences could affect the prevention benefits achieved.

Indeed, HCV epidemics vary widely between countries, with most of the HCV burden in high-income countries being due to needle and syringe sharing among people who inject drugs (PWID)(16, 17), while medical and community risk factors are important in most low and middle-income countries (LMICs)(18, 19). These epidemic differences will affect the prevention benefits achieved from a treat-all strategy.

We use dynamic HCV transmission modelling to determine the HCV infections averted (IA) per DAA treatment at a global, regional, and country-level for a random treat-all strategy, comparing it to treating other subgroups, and evaluating how the impact achieved depends on different country-specific factors. While other studies have investigated the morbidity and mortality benefits from different treatment allocations(13, 14), this study focuses on modelling the prevention of subsequent chronic HCV infections, comparing a treat-all policy to treating just PWID, individuals with cirrhosis, or those aged ≥35 years.

Methods

Model description

A dynamic, deterministic HCV transmission model was used to simulate each country-level HCV epidemic among the general population and PWID, incorporating population growth, age demographics, and HCV progression. Three age groups were modelled: 0–14, 15–34, and ≥35–year olds, with the middle age group selected to approximate the age range that individuals start injecting, using information from Degenhardt et al(20). New-borns enter the youngest group and age through the age groups. Adults (≥15 years) were stratified into individuals who had never injected drugs, PWID currently (referred to as PWID henceforth), and people who previously injected drugs (see supplementary Fig. 1 for a schematic diagram describing ageing and injecting drug use [IDU]). Only young adults (15–34-year olds) were assumed to initiate injecting, with PWID ceasing injecting at a fixed rate to become people who previously injected drugs.

Most individuals enter the model susceptible to infection, with HCV transmission either occurring due to ~~injecting drug use (~~IDU~~)~~ among PWID, or due to other risk factors among all individuals, representing medical/community risk factors. However, due to mother-to-child transmission of HCV, some individuals enter the model chronically infected with HCV(21). Once infected, individuals either spontaneously clear their infection and return to the susceptible class or develop life-long chronic infection. Chronically infected individuals progress through different HCV-related disease stages (chronic, compensated cirrhosis, and decompensated cirrhosis) with increased HCV-related mortality for individuals with decompensated cirrhosis.

Modelled HCV treatment can occur at rates dependent on the stage of infection, age, and injecting status. A proportion of treated individuals achieve a sustained virologic response (SVR), whereupon they become susceptible to re-infection (re-infection is assumed to occur at the same rate as primary infection, supplementary Fig. 2 gives a schematic of disease progression), whereas the remainder do not achieve SVR and remain chronically infected. Following successful treatment, no further disease progression occurs if they had chronic infection(22), but continued slower disease progression occurs among those with cirrhosis(22). All individuals die at age-specific death rates, with PWID experiencing elevated death due to drug-related mortality(23).

Model parameterization

The model was parameterized and calibrated using country-specific data from recent systematic reviews and United Nations (UN) datasets(2, 20, 24-32). Information on population sizes, age distributions, fertility rates, and mortality rates came from UN datasets, whilst HIV prevalence data (used solely for calculating the HCV vertical transmission rate which varies by HIV status, see the supplementary materials) were taken from the World Bank(33). Estimates for the proportion of the population that are PWID (among adults: 0.03%-4.19%) and antibody prevalence of HCV among PWID (5.5%-97.1%) and the general population (0.1%-13.1%) came from recent systematic reviews(2, 20), and other reviews where necessary (see supplementary materials). Table 1 gives the country-level prevalence estimates. Only USA, Egypt, and France have “two robust surveys”(2) (national general population cross-sectional surveys; supplementary materials give more information), with these data being used to model the dynamics of their HCV epidemics. For country-level HCV prevalence estimates (PWID and general population), antibody prevalence estimates were taken from reviews, and then adjusted using region-specific viraemic proportions(34, 35) to estimate the prevalence of chronic infection in the survey year. Country-level data (regional estimates used if no country-level data) on the current duration of injecting from the systematic

review by Degenhardt(20) were used to estimate the duration of injecting until cessation, applying wide uncertainty bounds (-50% to +100%) to account for uncertainty in how this variable relates to the real duration till cessation of injecting.

Historical treatment numbers were taken from a paper examining progress towards the WHO 2030 elimination targets(36) and a series of papers on the historical epidemiology of HCV in different countries(37-40). However, data for some countries were taken from other sources, discussed fully in the supplement. Little data are available on treatment numbers among PWID, so for simplicity we assumed similar levels of treatment in this group. Where data on treatment numbers were unavailable, then no treatments were assumed to occur. All key parameters had uncertainty, with bounds generally obtained directly from studies. Where uncertainty bounds were not available, a ±33% uncertainty range was applied, corresponding to the average level of uncertainty for parameters with uncertainty bounds.

Model calibration

The model was calibrated to 88 countries, accounting for 85% of the global population, 92% of the total population in high-income countries (HIC), and 83% in LMICs (2016 World Bank categories). The modelling only covered 43% of sub-Saharan Africa's population, 62% of the Middle East and North Africa, and 64% of Latin America, whilst covering >95% of the population of the remaining regions (supplementary Fig 3).

A four-step calibration method, using different sub-models, was used to calibrate the full model to data for each country, from 1990 onwards. For each step, we randomly sampled the various model parameters and calibration data from their uncertainty bounds, and then estimated other unknown model parameters through calibrating sequential sub-models. Samples were generated until 1000 full model fits were obtained for each country, with runs being rejected if they could not fit the calibration data described below.

In brief, for each sampled parameter set, we first used a population growth sub-model (sub-model 1) to calculate the average country-specific population growth rates between 1990-2015, calibrating to population sizes in 2015. Sub-model 1 was then adapted to include age demographics (sub-model 2) to estimate age-specific death rates in 2015, calibrating to data on the proportion of the population in the age-groups 0-14, 15-34, and ≥35 years. Sub-model 2 was then further adapted to include IDU (sub-model 3) to estimate initiation rates into IDU by calibrating to the country's population proportion of PWID among adults. Lastly, sub-model 3 was further extended to the full model to include HCV infection. Sampled and previously fitted parameters were used in the full model to estimate HCV transmission rates for PWID and the general population, calibrated to chronic prevalence estimates for the specific year where data was available for each country (between 1994-2015, with only four countries having pre-2000 estimates). The population growth rates between 1990 and 2015, age-specific death rates, the rate individuals initiate injecting, and HCV transmission rates for the general population and PWID were fitted, whilst all other parameters were taken from the literature (see supplementary table 3 for fitted parameters and supplementary tables 1 and 2 for model parameters informed by the literature, including their sources). Individual transmission risks in the general population (eg. due to unsafe medical injections) are not explicitly modelled as data to calibrate a global model with these parameters are unavailable. Therefore, we assume that the general population HCV transmission is due to a combination of medical (eg. unsafe medical

injections), social (eg. circumcision), and community (eg. barbering) factors(19, 41, 42). The supplementary materials fully describe the calibration methods and the model equations.

Due to global improvements in blood bank screening(43), and reductions in the re-use of medical syringes(19), country-level HCV epidemics were assumed to be declining over time. Consistent with a recent review and modelling of the global HCV epidemics over time(2), we assumed that the general population HCV prevalence in each country was decreasing by just over 1% per year, with wide sampling ranges (no decrease to 150% of this decrease) being associated with this estimate due to uncertainty in the data used to produce this decrease. This assumption was tested in sensitivity analyses. Based on synthesised data from Degenhardt's review(20), we assumed the HCV prevalence among PWID was stable between 1990 and the time of each countries HCV prevalence estimate. Similarly, the proportion of adults that are PWID was also assumed to be stable, except for Sub-Saharan African and Eastern European countries where it was assumed to be low in 1990 (25% of the recent country estimate) due to evidence suggesting IDU in these regions expanded later than in other settings(44).

Model analyses

The 1000 full model fits for each country were run over 2018-2038, firstly with that country's baseline level of treatment (counterfactual projections) and then with 50 additional individuals being treated in 2018, with the difference in the number of new infections between the paired runs being divided by 50 to give the IA per additional treatment over 20-years. Fifty treatments were chosen to give an estimate of the initial prevention benefit of further treatment scale-up while being small enough not to alter each country's ongoing epidemic trajectory. This gives an estimate of the initial prevention benefit of further treatment scale-up. Scenarios assumed the treated individuals were either selected randomly from all infected individuals, or selected from PWID, people with cirrhosis, or people ≥35 years old (infected individuals can overlap between categories). For each scenario and country, projections across the 1000 model fits were used to produce 95% credibility intervals (95%CrI) for all impact estimates. For each scenario, regional and global estimates of the IA per treatment were produced by weighting country-level estimates by that country's relative burden of HCV compared to the modelled regional and global burdens.

Univariable and multivariable regression models investigated which country-level characteristics (current population growth rate, population-attributable fraction of IDU to HCV transmission (the percentage of new HCV infections prevented 2018-2038 if the additional transmission risk among PWID was reduced to zero(45)), population proportion of PWID among adults, average duration of IDU, HCV prevalence among PWID and the general population) were associated with the number of IA per randomly allocated treatment and per treatment among PWID.

Sensitivity analyses

Sensitivity analyses considered the effect of specific assumptions in the model: assuming stable HCV epidemics instead of decreasing epidemics, assuming a recent increase in IDU in USA(46) in line with the on-going opioid epidemic, assuming longer-term epidemics of IDU in SSA and Eastern Europe instead of them recently evolving, assuming treatment rates are halved among PWID and doubled among people with cirrhosis (but overall allocating the same number of treatments), and assuming HCV epidemic trajectories vary based on regional data. We estimated the prevention impact of on-

going levels of treatment in each country by comparing the impact achieved over 20 years due to the treatments undertaken in 2018, compared to if they had not occurred in that year, but had in subsequent years. We examined the IA per treatment when only including the 66 countries with ≥2 of the key prevalence parameters scored as moderate or better (supplementary table 7).

The supplementary materials further discuss methods and the rationale underlying these assumptions, and the sensitivity analyses testing them.

Results

Globally, the model estimates 0.35 (95%CrI: 0.16, 0.61) IA per treatment over the next 20-years from treating people randomly. China, India, Nigeria, Pakistan, and Russia, which contain around 52% of infected individuals in the modelled countries, drive this global estimate. The estimated IA varies substantially across regions and countries (Fig 1; Table 2). The region with the lowest IA per randomly allocated treatment is Eastern Europe, 0.06 (95%CrI: -0.03, 0.20), while sub-Saharan Africa has the highest, 0.75 (95%CrI: 0.45, 1.10).

Table 2 and Fig 1 show the prevention benefit of randomly allocating treatment compared to targeting treatment to PWID, patients with cirrhosis, or people aged ≥35. Globally, treating PWID achieves the most prevention impact with 1.27 (95%CrI: 0.68, 2.04) IA per treatment. This ranges from as much as 4.82 (95%CrI: 1.98, 6.86) in Madagascar, to negative in Mauritius (–0.52 [95%CrI: –0.60, –0.14]) due to high levels of re-infection of PWID, although overall numbers of infected individuals still reduce because of the additional individuals cured through treatment. Globally, the IA per treatment given to individuals with cirrhosis (0.28 [95%CrI: 0.12, 0.49]) or are aged ≥35 years (0.30 [95%CrI: 0.12, 0.53]) is less but similar to what is achieved from randomly allocating treatment.

Determinants of impact

The IA per randomly allocated treatment (Table 3) is positively associated with a country's population growth-rate (Fig 2a) and the proportion of adults that are PWID, whereas it is negatively associated with the HCV prevalence in the general population and PWID (Fig 2b). The multivariable regression model's R^2-value is 0.58, indicating these variables explain most of the variation in estimated IA between countries.

Similarly, the number of IA per treatment allocated to PWID was positively associated with a country's population growth-rate (Fig 3a) and population proportion of PWID, and negatively associated with the prevalence of HCV among PWID (Fig 3b) and the general population (multivariable R^2-value: 0.77). Allocating treatment to PWID resulted in negative IA in eight (8%) countries, which had higher (≥61%) chronic HCV prevalence among PWID resulting in high modelled re-infection rates.

Sensitivity analyses

Sensitivity analyses (supplementary tables 10 and 11) show each strategy averts more infections if the general population HCV prevalence in each country is stable (0.55 [95%CrI: 0.36, 0.77] IA per treatment with random allocation) instead of decreasing (baseline projections). When assuming different regional epidemic trajectories, the global IA per randomly allocated treatment increases to 0.65 [95%CrI: 0.30, 1.10] as some countries were assumed to have stable or increasing epidemics. Assuming background treatment rates are halved among PWID and doubled for people with cirrhosis ~~reduces the~~produces a similar number of IA per extra randomly allocated treatment (0.~~21~~34 [95%CrI: 0.~~08~~14, 0.~~40~~60]) compared with the baseline projections. There are more IA per randomly allocated treatment when assuming increasing IDU in the USA since 2010(46) (1.02 [95%CrI: 0.30, 2.26] vs 0.60 [95%CrI: 0.24, 1.16] with a stable proportion of PWID).

Supplementary table 12 gives the projected number of IA from ongoing treatment rates in 2018 (around 1.5 million treatments globally) compared to if no treatments were given in 2018 but

resumed in 2019. This suggests that from these 1.5 million treatments, 525,764 (95%CrI: 243,948, 980,523) chronic HCV infections would be averted over the next 20 years, with similar numbers of IA per treatment being seen for each country and globally (0.34, 95%CI: 0.16, 0.63) as previously estimated for 50 randomly allocated treatments in 2017.

When only including the countries with ≥2 key prevalence parameters scored as moderate or better, the IA per randomly allocated treatment was similar, 0.35 (95%CI: 0.15, 0.60), to including all countries.

Discussion

Our modelling suggests that one infection will be prevented over the next 20-years for every three randomly allocated HCV treatments undertaken globally. The number of HCV infections that are averted will vary by region and country, with twenty randomly allocated treatments being needed to prevent one infection in Eastern Europe, but less than two in sub-Saharan Africa. Targeting treatment to people aged ≥35 or with cirrhosis is likely to produce similar prevention benefits. Targeting PWID could achieve greater impact, with over one infection being prevented for every PWID treated globally but with impact varying considerably by country and region. Results suggest the prevention impact of randomly allocating treatment or treating PWID will be greater in countries with high population growth but will be reduced in countries with high HCV prevalence among PWID, due to greater re-infection following treatment.

Strengths and limitations

This analysis's strength is the simulation of many country-level HCV epidemics covering 85% of the world's population. The differing role of IDU to each modelled HCV epidemic is captured, and differences in population demographics and growth. However, due to data limitations, over half of the world's countries are not represented, overwhelmingly LMICs, including only eight countries in Sub-Saharan Africa, possibly affecting regional and global results.

This study, commissioned by the WHO to focus on the prevention benefits of a treat-all policy, does not consider morbidity or mortality benefits. These outcomes have been considered in previous economic models, which emphasise the importance of treating individuals with cirrhosis for reducing the burden of liver-related deaths(13, 14). This model does not consider the impact of scaling up prevention interventions (eg. opiate substitution treatment [OST] and needle and syringe programs [NSP]) as the focus was the prevention benefits of treatment.

The modelling of so many countries necessitated the use of a generalizable model structure and standardized algorithm for calibrating the model to each country's epidemic. The model does not account for country's varying genotype(34), however, evidence suggests that new DAA regimens are pan-genotypic so this should not affect the results(47). HIV co-infection was not included in the model except for its effect on mother-to-child transmission(21). HIV co-infection will probably reduce survival in some countries, although recent increases in HIV treatment coverage has reduced this(48). We did not model transmission among men who have sex with men (MSM). This is unlikely to affect the results as although HCV prevalence among MSM is higher than among the general population, it is much lower than in PWID and partially due to IDU(49). Our model did not include

population migration due to data limitations. Migration could be a significant source of new HCV infections in some countries(50) (although possibly less than expected(51)), which could affect the prevention benefits of treatment. Our model gives general insights on the prevention benefits of treatment, and its variability and determinants, giving impetus to undertaking more detailed country-specific modelling.

Regarding historical treatment rates, numbers were unavailable for some countries, were frequently only available for one year, and were not stratified by IDU status or disease stage, necessitating various assumptions discussed in the supplementary materials and tested in sensitivity analyses. Countries are also at varying stages of treatment scale-up(7), therefore the extra 50 treatments given may impact differently across settings. We examined this in a sensitivity analysis on the impact of on-going treatment rates, suggesting similar IA per treatment.

The biggest limitation was the lack of high-quality data for some countries on the population proportion of PWID, and the prevalence of HCV in the general population and PWID. Countries with at least one estimate for each of these parameters from existing systematic reviews were included in this analysis; however, some data were old, used ambiguous methods, or had uncertain findings. Supplementary table 7 shows 46% of countries modelled had a general population HCV prevalence estimate with a low score(2). This was the case for 20% of country estimates for HCV prevalence among PWID(20), and 39% of estimates for the proportion of adults that inject drugs(20). Data and modelling for countries with higher-scored data estimates should be viewed with more confidence, with results from these countries giving a similar IA per randomly allocated treatment. Issues of data quality are partly due to the illicit and stigmatised nature of injecting, so estimates of PWID population sizes are often obtained indirectly. Additionally, there was little information on the on-going dynamics of HCV epidemics in most countries, with only three countries (Egypt, France, and USA) having robust data(2) (two surveys with similar methodology) on this, which our analyses showed could affect the number of IA(52). The main systematic reviews contributing data to this analysis were published in 2017, but most national data were older meaning they could pre-date recent changes that could affect transmission, such as upturns in injection-related HCV epidemics as has occurred in the USA(46). Due to these limitations, the models may not include recent changes in HCV epidemics. The effect of this was investigated in the USA, with sensitivity analyses suggesting greater IA when assuming an increased initiation of IDU after 2010. The model was not fit to age-specific HCV prevalence data due to a lack of data on this for many countries modelled. Where available, it was not necessarily robust enough to use, particularly for the youngest age group where the number of survey participants were often low or the age group was excluded entirely. These analyses highlight the importance of improving country-level information on the on-going trajectory of HCV epidemics to better understand the likely impact of treatment scale-up; this will also be crucial for assessing progress to the WHO HCV elimination targets.

Comparison to other studies

To our knowledge, this study is the first to evaluate the prevention impact of different HCV treatment allocation strategies across global settings, the first to produce a global estimate for the IA per treatment, and the first to determine how country-level factors affect the impact achieved. Other modelling analyses have considered the prevention benefits of HCV treatment among PWID, MSM, and the general population(12, 13, 15, 52-59). Some analyses of PWID HCV epidemics have

also suggested that less prevention benefit will be achieved in settings with higher or increasing HCV prevalence among PWID(12, 13, 46, 60). However, no study has undertaken similar analyses for generalized HCV epidemic settings.

Implications

These analyses show that globally, a moderate prevention impact (one infection prevented per three treatments undertaken) can be achieved with a treat-all strategy, with greatest benefit achieved in countries with high population growth. These findings are useful for policy-makers as they provide an understanding of the prevention benefits of widespread treatment scale-up when planning for the WHO 2030 HCV elimination targets(6). The analyses suggest that countries in some regions, such as sub-Saharan Africa and South Asia, could achieve greater prevention benefits from scaling up treatment than other regions, such as Eastern Europe and Latin America, due to having growing populations and generalized epidemics. However, many countries lack the resources to treat HCV(61), or screening may present a barrier to treatment scale-up due to their HCV epidemics being generalised(16). This issue will be particularly pertinent for countries with high burdens of other infectious diseases, where policy-makers may focus their resources on more acute diseases rather than HCV. Only with substantial donor support, or considerable improvements in access to HCV DAA therapies and diagnostic tests, will such countries be able to substantially scale-up treatment for HCV.

Importantly, our analyses also re-emphasized the prevention benefits of targeting PWID, as PWID were the subgroup for whom treatment produced the most IA globally and in most countries. This is due to the higher likelihood of PWID transmitting HCV relative to other subgroups(62). However, PWID comprise only a fraction of the overall HCV burden globally(63), and a very small fraction of both incidence and prevalence for some countries such as Nigeria. Therefore, ~~so~~ any elimination strategy must also target other groups, such as those with a history of receiving blood transfusions, especially in settings with high rates of infection due to nosocomial factors, such as Pakistan and Egypt(64, 65). Additionally, if HCV prevalence is high among PWID then no infections may be averted from moderate treatment levels among PWID, due to high re-infection rates. In these scenarios, treatment rates must be high among PWID, and/or other HCV prevention interventions for PWID (OST and NSP) need to be scaled up to reduce re-infection risks(66). Either way, these insights emphasize the need to allocate resources to treating PWID, either due to the greater prevention benefits achieved and/or to gain control of the epidemic among PWID; crucial for achieving elimination.

For preventing onwards transmission, this paper's findings support WHO's new guidelines for a treat-all strategy(9), with special emphasis also being placed on treating PWID for whom the most prevention benefit is achieved. However, in many settings, particularly low- or middle-income countries, targeting treatment solely to PWID would not be enough to meet the WHO's elimination target for incidence. A treat-all strategy ~~Such a strategy~~ would reduce practical obstacles to treatment, such as screening to prioritise individuals with advanced disease, and could be considered more equitable by allowing all those who seek treatment to access it. There are other issues to consider, mainly surrounding resourcing for the costs of testing and treatment and ensuring that those with progressed disease are treated. If these issues can be dealt with, our

analyses suggest that a widespread treat-all strategy will achieve considerable prevention benefits in most settings.

Table 1: Country-level sampled ranges for antibody prevalence of HCV among the general population and people who inject drugs (PWID), as well as the prevalence of injecting drug use and their duration of injecting drug use. Prevalence ranges are taken from the literature, and where they were not available ranges of ±33% are used. Ranges for injecting duration are taken as 50% and 200% of the estimate for the current duration of injecting.

Country	Year for general population anti-HCV prevalence estimate	Prevalence			Injecting drug use duration (years)[6]
		Anti-HCV among general population (%)	Anti-HCV prevalence among PWID (%)	% of adults that are PWID	
Afghanistan	2007	1.10% (0.40%, 1.92%)	37.8% (27.5%, 48.1%)	0.80% (0.50%, 1.09%)	6.8 (3.4, 13.6)
Albania	2008	3.00% (2.01%, 3.99%)	34.0% (27.5%, 41.0%)	0.42% (0.28%, 0.56%)	12.4 (6.2, 24.8)
Argentina	2007	1.50% (0.32%, 2.00%)	54.6% (51.1%, 58.1%)	0.29% (0.29%, 0.30%)	13.2 (6.6, 26.4)
Armenia	2010	4.00% (2.68%, 5.32%)	42.7% (29.3%, 56.1%)	0.62% (0.41%, 1.35%)	11.8 (5.9, 23.6)
Australia	2012	1.30% (1.20%, 1.85%)	53.5% (50.2%, 56.9%)	0.60% (0.43%, 0.76%)	15.4 (7.7, 30.8)
Austria	2008	0.50% (0.10%, 0.70%)	60.9% (54.8%, 67.0%)	0.32% (0.22%, 0.42%)	13.0 (6.5, 26.0)
Azerbaijan	2010	3.70% (2.48%, 4.92%)	62.1% (47.1%, 77.2%)	0.61% (0.49%, 0.74%)	8.8 (4.4, 17.6)
Bangladesh	2010	1.26% (0.20%, 2.23%)	33.9% (22.4%, 45.4%)	0.07% (0.06%, 0.07%)	6.0 (3.0, 12.0)
Belarus	2006	1.26% (0.86%, 2.85%)	58.3% (43.3%, 73.3%)	0.59% (0.22%, 0.96%)	10.9 (5.5, 21.8)
Belgium	1994	0.87% (0.12%, 1.10%)	58.4% (47.0%, 69.7%)	0.35% (0.24%, 0.49%)	13.3 (6.7, 26.6)
Bosnia	2008	0.10% (0.07%, 0.13%)	39.9% (27.5%, 52.4%)	0.17% (0.11%, 0.23%)	15.0 (7.5, 30.0)
Brazil	2007	1.38% (1.12%, 1.64%)	63.9% (60.5%, 67.3%)	0.67% (0.51%, 0.87%)	13.2 (6.6, 26.4)
Bulgaria	2012	1.50% (0.70%, 2.43%)	68.7% (64.3%, 73.0%)	0.38% (0.30%, 0.45%)	9.0 (4.5, 18.0)
Canada	2011	0.96% (0.61%, 1.34%)	70.6% (60.1%, 93.9%)	0.39% (0.31%, 0.47%)	14.3 (7.2, 28.6)
China	2015	1.21% (0.93%, 1.49%)	43.1% (27.5%, 58.6%)	0.25% (0.19%, 0.31%)	7.1 (3.6, 14.2)
Croatia	2011	0.90% (0.50%, 1.40%)	36.7% (28.1%, 45.3%)	0.23% (0.18%, 0.29%)	13.5 (6.8, 27.0)
Cyprus	2001	0.56% (0.45%, 1.87%)	49.7% (44.4%, 55.0%)	0.08% (0.04%, 0.12%)	8.8 (4.4, 17.6)
Czech Republic	2012	0.57% (0.20%, 0.70%)	18.3% (14.5%, 22.1%)	0.64% (0.61%, 0.67%)	11.8 (5.9, 23.6)
Denmark	2007	0.63% (0.48%, 0.72%)	42.6% (36.1%, 49.1%)	0.45% (0.35%, 0.52%)	18.2 (9.1, 36.4)
Egypt	2015	10.00% (9.50%, 10.50%)	49.4% (35.8%, 63.0%)	0.21% (0.13%, 0.28%)	5.2 (2.6, 10.4)
Estonia	2013	1.97% (1.50%, 2.00%)	79.2% (67.4%, 91.0%)	0.94% (0.69%, 1.73%)	8.1 (4.1, 16.2)
Finland	2013	0.68% (0.60%, 0.90%)	73.7% (69.9%, 77.2%)	0.46% (0.41%, 0.67%)	12.4 (6.2, 24.8)
France	2004	0.84% (0.45%, 1.10%)	64.0% (60.8%, 67.0%)	0.20% (0.16%, 0.23%)	12.4 (6.2, 24.8)
FYROM	2008	0.50% (0.34%, 0.67%)	62.2% (59.4%, 64.9%)	0.16% (0.11%, 0.21%)	12.4 (6.2, 24.8)
Georgia	2015	5.40% (4.51%, 6.32%)	69.1% (58.0%, 80.2%)	4.19% (0.48%, 7.90%)	14.1 (7.1, 28.2)
Germany	2012	0.58% (0.30%, 0.90%)	65.0% (60.6%, 69.4%)	0.24% (0.03%, 0.45%)	13.9 (7.0, 27.8)
Ghana	2014	2.10% (1.20%, 5.50%)	40.1% (34.8%, 45.4%)	0.05% (0.03%, 0.07%)	10.0 (5.0, 20.0)
Greece	2011	1.79% (0.50%, 2.61%)	65.7% (61.8%, 69.5%)	0.07% (0.06%, 0.09%)	11.7 (5.9, 23.4)
Hungary	2014	0.70% (0.40%, 2.70%)	46.4% (30.4%, 62.8%)	0.06% (0.03%, 0.08%)	9.6 (4.8, 19.2)
Iceland	2013	0.41% (0.33%, 0.48%)	63.0% (59.8%, 66.2%)	0.24% (0.16%, 0.32%)	7.0 (3.5, 14.0)
India	2013	0.84% (0.50%, 1.50%)	40.0% (33.9%, 46.1%)	0.02% (0.01%, 0.03%)	7.2 (3.6, 14.4)
Indonesia	2007	0.80% (0.10%, 1.70%)	89.2% (85.3%, 92.3%)	0.11% (0.09%, 0.13%)	7.1 (3.6, 14.2)
Iran	2006	0.50% (0.20%, 1.00%)	44.1% (28.2%, 59.9%)	0.28% (0.19%, 0.37%)	8.2 (4.1, 16.4)
Ireland	2010	0.70% (0.67%, 1.60%)	74.6% (72.3%, 76.9%)	0.27% (0.20%, 0.33%)	12.4 (6.2, 24.8)
Israel	2006	1.96% (0.90%, 2.10%)	45.3% (38.1%, 52.6%)	0.41% (0.27%, 0.55%)	14.0 (7.0, 28.0)
Italy	2001	2.43% (1.60%, 7.30%)	57.9% (52.5%, 63.3%)	0.83% (0.57%, 1.14%)	9.0 (4.5, 18.0)
Japan	2011	0.98% (0.49%, 2.20%)	64.8% (55.0%, 74.5%)	0.47% (0.36%, 0.58%)	7.3 (3.7, 14.6)

Kazakhstan	2010	3.20% (1.30%, 4.26%)	58.8% (54.0%, 63.6%)	0.96% (0.64%, 1.42%)	5.0 (2.5, 10.0)
Kenya	2007	0.76% (0.20%, 1.01%)	16.4% (10.9%, 23.3%)	0.12% (0.03%, 0.20%)	5.3 (2.7, 10.6)
Kyrgyzstan	2010	2.45% (1.60%, 6.70%)	43.9% (40.6%, 47.2%)	0.74% (0.50%, 1.11%)	6.3 (3.2, 12.6)
Latvia	2008	2.40% (1.70%, 3.30%)	74.4% (67.6%, 81.2%)	0.92% (0.73%, 1.17%)	9.1 (4.6, 18.2)
Lebanon	2011	0.21% (0.11%, 0.70%)	23.4% (15.3%, 33.3%)	0.14% (0.09%, 0.19%)	5.2 (2.6, 10.4)
Libya	2005	1.20% (1.10%, 1.30%)	94.5% (91.5%, 96.7%)	0.05% (0.01%, 0.10%)	5.2 (2.6, 10.4)
Lithuania	2010	1.96% (1.21%, 2.71%)	41.1% (38.1%, 44.2%)	0.22% (0.12%, 0.34%)	10.0 (5.0, 20.0)
Luxembourg	2006	1.34% (0.56%, 1.61%)	81.3% (76.2%, 85.8%)	0.57% (0.45%, 0.69%)	12.4 (6.2, 24.8)
Madagascar	2004	1.20% (0.75%, 1.72%)	5.5% (2.1%, 9.0%)	0.12% (0.02%, 0.59%)	7.8 (3.9, 15.6)
Malaysia	2011	1.90% (0.30%, 7.70%)	67.1% (62.9%, 71.1%)	1.33% (1.11%, 1.56%)	13.9 (7.0, 27.8)
Malta	2010	0.36% (0.26%, 0.60%)	25.2% (13.1%, 37.3%)	0.26% (0.17%, 0.35%)	12.4 (6.2, 24.8)
Mauritius	2010	2.10% (1.41%, 2.79%)	97.1% (96.0%, 98.1%)	0.78% (0.39%, 1.54%)	14.0 (7.0, 28.0)
Mexico	2000	1.40% (1.10%, 1.60%)	95.3% (93.3%, 97.3%)	0.18% (0.12%, 0.25%)	16.1 (8.1, 32.2)
Moldova	2010	4.46% (2.30%, 4.46%)	50.1% (34.1%, 66.1%)	0.40% (0.25%, 0.54%)	12.7 (6.4, 25.4)
Montenegro	2008	1.20% (0.80%, 1.60%)	43.4% (39.8%, 47.1%)	0.40% (0.27%, 0.53%)	6.0 (3.0, 12.0)
Morocco	2008	1.20% (1.10%, 1.93%)	53.9% (33.7%, 74.0%)	0.13% (0.07%, 0.20%)	10.0 (5.0, 20.0)
Mozambique	2011	1.30% (0.10%, 6.90%)	67.1% (62.9%, 71.2%)	0.20% (0.00%, 0.41%)	7.8 (3.9, 15.6)
Myanmar	2009	1.69% (0.95%, 2.66%)	29.5% (26.9%, 32.2%)	0.48% (0.32%, 0.65%)	3.4 (1.7, 6.8)
Nepal	2010	0.64% (0.43%, 0.85%)	44.5% (30.8%, 58.2%)	0.20% (0.19%, 0.21%)	5.2 (2.6, 10.4)
Netherlands	2009	0.22% (0.07%, 0.37%)	55.3% (49.7%, 60.9%)	0.03% (0.02%, 0.04%)	12.4 (6.2, 24.8)
New Zealand	2013	1.43% (0.81%, 2.15%)	71.9% (63.2%, 80.6%)	0.73% (0.49%, 0.97%)	15.4 (7.7, 30.8)
Nigeria	2012	2.20% (2.10%, 2.50%)	5.8% (3.5%, 8.9%)	0.35% (0.23%, 0.47%)	8.0 (4.0, 16.0)
Norway	2012	0.55% (0.45%, 0.70%)	64.8% (60.4%, 69.1%)	0.24% (0.21%, 0.29%)	14.0 (7.0, 28.0)
Pakistan	2008	4.80% (4.70%, 5.10%)	36.5% (5.1%, 79.1%)	0.37% (0.32%, 0.42%)	5.1 (2.6, 10.2)
Philippines	2003	0.94% (0.33%, 2.00%)	35.2% (15.9%, 54.5%)	0.04% (0.03%, 0.05%)	6.8 (3.4, 13.6)
Poland	2009	0.86% (0.59%, 1.14%)	58.7% (55.1%, 66.2%)	0.27% (0.18%, 0.36%)	14.4 (7.2, 28.8)
Portugal	1995	1.50% (0.47%, 2.87%)	87.7% (80.5%, 95.0%)	0.22% (0.19%, 0.25%)	12.4 (6.2, 24.8)
Romania	2007	3.23% (2.94%, 3.55%)	83.8% (80.6%, 87.1%)	0.62% (0.46%, 0.84%)	9.8 (4.9, 19.6)
Russia	2010	4.10% (1.16%, 5.60%)	68.7% (59.6%, 77.9%)	1.78% (0.94%, 2.71%)	7.6 (3.8, 15.2)
Saudi Arabia	2011	0.51% (0.41%, 0.61%)	77.8% (73.2%, 81.9%)	0.20% (0.13%, 0.27%)	5.2 (2.6, 10.4)
Senegal	2009	1.00% (0.00%, 4.60%)	39.3% (31.1%, 47.9%)	0.08% (0.05%, 0.11%)	7.8 (3.9, 15.6)
Serbia	2008	0.50% (0.34%, 0.67%)	25.9% (22.1%, 29.7%)	0.49% (0.41%, 0.58%)	8.8 (4.4, 17.6)
Slovakia	2011	1.40% (0.88%, 1.98%)	56.1% (35.6%, 76.7%)	0.49% (0.35%, 0.89%)	11.8 (5.9, 23.6)
Slovenia	2015	0.40% (0.30%, 0.50%)	30.5% (26.4%, 34.5%)	0.42% (0.30%, 0.55%)	12.4 (6.2, 24.8)
Spain	2012	1.50% (0.40%, 2.64%)	71.0% (69.5%, 72.5%)	0.08% (0.05%, 0.10%)	11.2 (5.6, 22.4)
Sweden	2012	0.56% (0.47%, 0.69%)	81.7% (79.6%, 83.6%)	0.13% (0.03%, 0.62%)	21.0 (10.5, 42.0)
Switzerland	1998	1.55% (0.80%, 1.75%)	74.6% (69.3%, 79.4%)	0.24% (0.19%, 0.29%)	12.4 (6.2, 24.8)
Syria	2004	2.80% (0.60%, 3.72%)	60.5% (40.5%, 80.5%)	0.07% (0.04%, 0.09%)	5.2 (2.6, 10.4)
Taiwan	2000	3.28% (2.50%, 8.60%)	91.0% (89.5%, 92.4%)	0.30% (0.20%, 0.40%)	15.5 (7.8, 31.0)
Tajikistan	2010	3.06% (1.10%, 6.70%)	61.3% (56.8%, 65.6%)	0.45% (0.30%, 0.66%)	5.9 (3.0, 11.8)
Tanzania	2013	2.70% (0.20%, 7.80%)	27.7% (22.4%, 33.5%)	1.24% (0.72%, 1.76%)	4.3 (2.2, 8.6)
Thailand	2014	0.94% (0.75%, 3.66%)	88.5% (82.6%, 92.9%)	0.11% (0.03%, 0.18%)	7.3 (3.7, 14.6)
Tunisia	1996	1.27% (0.20%, 1.70%)	29.1% (25.7%, 32.6%)	0.21% (0.14%, 0.29%)	5.2 (2.6, 10.4)
Turkey	2009	0.95% (0.60%, 2.10%)	44.9% (41.7%, 48.2%)	0.42% (0.28%, 0.56%)	4.0 (2.0, 8.0)
Turkmenistan	2010	5.55% (1.10%, 6.70%)	60.6% (46.2%, 75.0%)	0.40% (0.27%, 0.53%)	5.9 (3.0, 11.8)
UK	2005	0.50% (0.40%, 0.75%)	46.0% (36.8%, 55.2%)	0.39% (0.38%, 0.42%)	10.0 (5.0, 20.0)

Ukraine	2010	3.58% (0.86%, 4.46%)	53.9% (49.2%, 58.7%)	0.97% (0.52%, 1.79%)	12.2 (6.1, 24.4)
Uruguay	2010	1.00% (0.67%, 1.33%)	21.9% (19.0%, 24.8%)	0.30% (0.10%, 0.87%)	13.2 (6.6, 26.4)
USA	2007	1.30% (1.20%, 1.50%)	53.1% (38.1%, 68.0%)	1.40% (0.57%, 1.88%)	16.2 (8.1, 32.4)
Uzbekistan	2000	13.10% (6.40%, 13.11%)	51.7% (46.8%, 56.6%)	0.47% (0.32%, 0.70%)	5.9 (3.0, 11.8)
Viet Nam	2012	1.49% (1.20%, 2.00%)	58.3% (42.7%, 74.0%)	0.25% (0.19%, 0.31%)	5.8 (2.9, 11.6)

Table 2: The number of chronic hepatitis C virus infections averted per treatment over 20 years (2018-2038) for the different treatment allocation scenarios, for each country, region and globally, with 95% credibility intervals.

	Chronic hepatitis C virus infections averted per treatment for different allocation strategies			
Country	**Random (treat-all)**	**PWID***	**People with cirrhosis**	**People aged ≥35 years**
Global	**0.35 (0.16, 0.61)**	**1.27 (0.68, 2.04)**	**0.28 (0.12, 0.49)**	**0.30 (0.12, 0.53)**
Central Asia	**0.32 (0.14, 0.56)**	**1.66 (1.25, 2.29)**	**0.24 (0.09, 0.43)**	**0.26 (0.08, 0.45)**
Kazakhstan	0.26 (0.18, 0.40)	1.42 (1.08, 2.38)	0.14 (0.08, 0.26)	0.16 (0.08, 0.28)
Kyrgyzstan	0.42 (0.24, 0.62)	2.14 (1.66, 2.78)	0.30 (0.12, 0.48)	0.30 (0.12, 0.48)
Tajikistan	0.50 (0.24, 0.76)	1.80 (1.36, 2.32)	0.38 (0.14, 0.60)	0.38 (0.14, 0.60)
Turkmenistan	0.40 (0.20, 0.64)	1.66 (1.10, 2.40)	0.30 (0.12, 0.50)	0.32 (0.14, 0.54)
Uzbekistan	0.30 (0.10, 0.56)	1.66 (1.26, 2.22)	0.24 (0.08, 0.44)	0.26 (0.06, 0.46)
Eastern Europe	**0.06 (-0.03, 0.20)**	**0.14 (-0.10, 0.72)**	**0.05 (-0.02, 0.14)**	**0.06 (-0.02, 0.16)**
Armenia	0.12 (0.02, 0.26)	0.50 (0.12, 1.02)	0.08 (0.02, 0.20)	0.08 (0.02, 0.22)
Azerbaijan	0.24 (0.06, 0.46)	0.28 (-0.08, 0.76)	0.20 (0.06, 0.38)	0.22 (0.06, 0.44)
Belarus	0.00 (-0.10, 0.14)	-0.14 (-0.36, 0.34)	0.00 (-0.06, 0.12)	0.00 (-0.06, 0.14)
Bosnia	0.00 (-0.12, 0.14)	0.02 (-0.18, 0.32)	0.00 (-0.10, 0.08)	0.00 (-0.10, 0.10)
Bulgaria	0.02 (-0.04, 0.10)	-0.02 (-0.20, 0.50)	0.00 (-0.02, 0.10)	0.02 (-0.02, 0.12)
Czech Republic	0.80 (0.54, 1.46)	2.48 (1.90, 3.24)	0.50 (0.28, 1.02)	0.60 (0.36, 1.20)
Estonia	0.40 (0.08, 0.80)	0.68 (0.08, 1.48)	0.28 (0.06, 0.62)	0.32 (0.08, 0.70)
Georgia	0.40 (0.14, 0.72)	0.74 (0.48, 1.06)	0.32 (0.12, 0.58)	0.34 (0.12, 0.62)
Hungary	0.20 (0.06, 0.42)	0.94 (0.40, 1.68)	0.16 (0.04, 0.36)	0.18 (0.04, 0.38)
Latvia	0.06 (-0.06, 0.26)	0.08 (-0.20, 0.70)	0.04 (-0.04, 0.18)	0.06 (-0.04, 0.20)
Lithuania	0.18 (0.08, 0.36)	0.88 (0.62, 1.30)	0.14 (0.06, 0.30)	0.16 (0.06, 0.32)
Moldova	0.14 (0.02, 0.30)	0.34 (-0.04, 0.88)	0.10 (0.00, 0.24)	0.12 (0.00, 0.28)
Poland	0.10 (0.00, 0.26)	0.16 (-0.02, 0.38)	0.08 (0.00, 0.22)	0.10 (0.00, 0.26)
Romania	-0.02 (-0.08, 0.06)	-0.26 (-0.38, 0.24)	0.00 (-0.06, 0.06)	0.00 (-0.06, 0.08)
Russia	0.02 (-0.06, 0.14)	0.02 (-0.22, 0.66)	0.02 (-0.04, 0.08)	0.02 (-0.04, 0.10)
Slovakia	0.08 (-0.06, 0.28)	0.12 (-0.24, 0.70)	0.04 (-0.04, 0.20)	0.06 (-0.04, 0.24)
Ukraine	0.10 (0.06, 0.22)	0.48 (0.30, 1.02)	0.06 (0.02, 0.16)	0.08 (0.04, 0.18)
Australasia	**0.26 (0.13, 0.49)**	**0.54 (0.29, 1.00)**	**0.21 (0.11, 0.41)**	**0.22 (0.11, 0.43)**
Australia	0.24 (0.14, 0.40)	0.54 (0.34, 0.92)	0.20 (0.12, 0.34)	0.20 (0.12, 0.34)
New Zealand	0.34 (0.06, 0.90)	0.52 (0.06, 1.34)	0.26 (0.04, 0.72)	0.30 (0.04, 0.80)
East & Southeast Asia	**0.26 (0.09, 0.49)**	**1.26 (0.70, 2.08)**	**0.19 (0.04, 0.39)**	**0.21 (0.04, 0.44)**
China	0.24 (0.10, 0.44)	1.40 (0.82, 2.26)	0.18 (0.04, 0.36)	0.20 (0.04, 0.40)
Indonesia	0.12 (-0.04, 0.36)	-0.10 (-0.26, 0.10)	0.12 (-0.02, 0.30)	0.12 (-0.02, 0.34)
Japan	0.46 (0.18, 0.88)	1.30 (0.68, 2.18)	0.32 (0.10, 0.66)	0.36 (0.12, 0.72)
Malaysia	0.32 (0.10, 0.56)	0.58 (0.26, 0.94)	0.26 (0.06, 0.46)	0.28 (0.08, 0.52)
Myanmar	0.30 (0.18, 0.50)	2.56 (1.96, 3.88)	0.18 (0.06, 0.34)	0.18 (0.06, 0.38)
Philippines	0.38 (0.16, 0.64)	2.14 (1.14, 3.68)	0.30 (0.12, 0.52)	0.34 (0.14, 0.56)
Taiwan	0.06 (-0.02, 0.26)	-0.08 (-0.24, 0.14)	0.06 (-0.02, 0.22)	0.06 (0.00, 0.26)
Thailand	0.16 (0.00, 0.38)	0.00 (-0.18, 0.22)	0.14 (0.00, 0.32)	0.16 (0.00, 0.36)
Viet Nam	0.24 (0.06, 0.44)	0.90 (0.40, 1.58)	0.18 (0.02, 0.34)	0.20 (0.02, 0.38)
South Asia	**0.49 (0.25, 0.76)**	**1.86 (0.96, 2.75)**	**0.41 (0.21, 0.63)**	**0.43 (0.21, 0.67)**
Afghanistan	0.86 (0.34, 1.34)	2.14 (1.16, 3.36)	0.62 (0.16, 1.02)	0.66 (0.18, 1.02)
Bangladesh	0.40 (0.20, 0.66)	1.90 (1.14, 2.92)	0.32 (0.16, 0.54)	0.34 (0.16, 0.56)
India	0.44 (0.22, 0.70)	1.74 (1.26, 2.48)	0.38 (0.20, 0.58)	0.40 (0.20, 0.64)
Iran	0.32 (0.10, 0.64)	0.98 (0.38, 1.86)	0.22 (0.04, 0.46)	0.26 (0.06, 0.52)

Nepal	0.30 (0.08, 0.56)	1.06 (0.46, 1.94)	0.22 (0.02, 0.42)	0.24 (0.04, 0.46)
Pakistan	0.58 (0.32, 0.86)	2.08 (0.50, 3.14)	0.48 (0.26, 0.72)	0.50 (0.26, 0.74)
North America	**0.58 (0.22, 1.13)**	**1.04 (0.44, 2.00)**	**0.46 (0.18, 0.90)**	**0.50 (0.20, 0.99)**
Canada	0.30 (-0.06, 0.72)	0.48 (-0.28, 1.28)	0.24 (-0.04, 0.58)	0.26 (-0.04, 0.64)
USA	0.60 (0.24, 1.16)	1.08 (0.50, 2.06)	0.48 (0.20, 0.92)	0.52 (0.22, 1.02)
Western Europe	**0.32 (0.13, 0.68)**	**0.91 (0.51, 1.62)**	**0.24 (0.09, 0.53)**	**0.27 (0.1, 0.58)**
Albania	0.10 (0.04, 0.24)	0.96 (0.72, 1.36)	0.08 (0.02, 0.18)	0.08 (0.02, 0.20)
Austria	0.66 (0.38, 1.08)	1.24 (0.72, 1.94)	0.50 (0.26, 0.84)	0.56 (0.28, 0.94)
Belgium	0.26 (0.06, 0.70)	0.74 (0.20, 1.36)	0.18 (0.02, 0.54)	0.20 (0.04, 0.60)
Croatia	0.16 (0.06, 0.32)	1.00 (0.70, 1.44)	0.10 (0.04, 0.24)	0.12 (0.04, 0.26)
Cyprus	0.32 (0.10, 0.56)	1.36 (0.88, 1.96)	0.24 (0.06, 0.44)	0.28 (0.08, 0.50)
Denmark	0.38 (0.28, 0.52)	1.06 (0.80, 1.42)	0.26 (0.16, 0.40)	0.30 (0.20, 0.46)
FYROM	0.08 (0.04, 0.22)	0.32 (0.20, 0.48)	0.04 (0.02, 0.18)	0.06 (0.02, 0.20)
Finland	0.06 (-0.02, 0.16)	0.14 (-0.04, 0.68)	0.04 (-0.02, 0.10)	0.04 (0.00, 0.12)
France	0.28 (0.14, 0.60)	0.76 (0.46, 1.40)	0.22 (0.12, 0.46)	0.24 (0.12, 0.50)
Germany	0.40 (0.18, 0.80)	0.88 (0.54, 1.38)	0.30 (0.12, 0.62)	0.34 (0.14, 0.70)
Greece	0.22 (0.04, 0.42)	0.42 (0.20, 0.70)	0.18 (0.04, 0.34)	0.20 (0.04, 0.40)
Iceland	0.26 (0.18, 0.38)	0.70 (0.44, 1.16)	0.18 (0.14, 0.26)	0.20 (0.14, 0.28)
Ireland	0.22 (0.06, 0.44)	0.42 (0.14, 0.80)	0.18 (0.04, 0.36)	0.20 (0.04, 0.40)
Italy	0.24 (0.08, 0.50)	0.86 (0.54, 1.60)	0.16 (0.06, 0.36)	0.18 (0.06, 0.40)
Luxembourg	0.94 (0.28, 1.60)	1.50 (0.54, 2.52)	0.76 (0.22, 1.30)	0.82 (0.24, 1.38)
Malta	0.36 (0.20, 0.64)	1.12 (0.60, 2.18)	0.28 (0.16, 0.48)	0.32 (0.18, 0.54)
Montenegro	0.12 (0.08, 0.22)	1.00 (0.70, 2.00)	0.06 (0.04, 0.14)	0.06 (0.04, 0.16)
Netherlands	0.28 (0.12, 0.58)	1.00 (0.38, 1.76)	0.24 (0.10, 0.48)	0.26 (0.10, 0.52)
Norway	0.64 (0.40, 0.94)	1.32 (0.90, 1.82)	0.50 (0.28, 0.74)	0.56 (0.32, 0.82)
Portugal	0.24 (0.06, 0.46)	0.44 (-0.14, 0.80)	0.20 (0.06, 0.40)	0.22 (0.06, 0.42)
Serbia	0.30 (0.22, 0.38)	1.42 (1.12, 2.20)	0.14 (0.10, 0.20)	0.18 (0.12, 0.24)
Slovenia	0.52 (0.38, 0.74)	1.50 (1.14, 2.18)	0.36 (0.24, 0.54)	0.42 (0.28, 0.62)
Spain	0.20 (0.08, 0.50)	0.70 (0.38, 1.12)	0.18 (0.06, 0.44)	0.20 (0.06, 0.46)
Sweden	0.62 (0.10, 1.18)	0.92 (0.00, 1.52)	0.52 (0.08, 1.00)	0.56 (0.10, 1.08)
Switzerland	0.38 (0.18, 0.64)	0.86 (0.52, 1.32)	0.30 (0.16, 0.52)	0.34 (0.16, 0.56)
UK	0.50 (0.22, 1.22)	0.96 (0.38, 2.04)	0.36 (0.14, 0.94)	0.40 (0.16, 1.04)
Sub Saharan Africa	**0.75 (0.45, 1.10)**	**2.30 (1.38, 3.38)**	**0.60 (0.33, 0.89)**	**0.57 (0.33, 0.86)**
Ghana	0.66 (0.40, 0.98)	1.94 (1.40, 2.64)	0.54 (0.32, 0.80)	0.54 (0.34, 0.80)
Kenya	0.68 (0.38, 1.04)	3.74 (2.22, 5.82)	0.50 (0.26, 0.80)	0.48 (0.26, 0.76)
Madagascar	0.76 (0.44, 1.16)	4.82 (1.98, 6.86)	0.60 (0.34, 0.94)	0.62 (0.36, 0.94)
Mauritius	-0.10 (-0.26, 0.10)	-0.52 (-0.60, -0.14)	-0.06 (-0.18, 0.12)	-0.04 (-0.18, 0.14)
Mozambique	0.62 (0.28, 0.96)	0.54 (0.20, 1.00)	0.50 (0.22, 0.80)	0.44 (0.20, 0.72)
Nigeria	0.76 (0.46, 1.12)	2.02 (1.04, 3.18)	0.62 (0.38, 0.92)	0.60 (0.36, 0.88)
Senegal	0.76 (0.46, 1.14)	1.94 (1.16, 2.98)	0.62 (0.38, 0.94)	0.62 (0.38, 0.90)
Tanzania	0.84 (0.54, 1.18)	3.20 (2.34, 4.26)	0.62 (0.30, 0.90)	0.58 (0.30, 0.90)
Latin America	**0.19 (0.03, 0.40)**	**0.18 (-0.01, 0.40)**	**0.15 (0.02, 0.32)**	**0.17 (0.02, 0.37)**
Argentina	0.24 (0.06, 0.46)	0.60 (0.36, 0.90)	0.18 (0.04, 0.36)	0.22 (0.04, 0.42)
Brazil	0.22 (0.08, 0.40)	0.42 (0.20, 0.68)	0.16 (0.04, 0.32)	0.18 (0.04, 0.36)
Mexico	0.12 (-0.08, 0.36)	-0.50 (-0.60, -0.38)	0.12 (-0.04, 0.32)	0.14 (-0.04, 0.36)
Uruguay	0.28 (0.12, 0.46)	1.60 (1.16, 2.28)	0.20 (0.06, 0.34)	0.22 (0.08, 0.40)
Middle East & North Africa	**0.20 (0.09, 0.41)**	**0.84 (0.50, 1.39)**	**0.18 (0.08, 0.35)**	**0.19 (0.08, 0.36)**
Egypt	0.18 (0.08, 0.38)	0.78 (0.46, 1.26)	0.18 (0.08, 0.34)	0.18 (0.08, 0.34)
Israel	0.62 (0.38, 0.88)	1.86 (1.40, 2.42)	0.48 (0.28, 0.70)	0.54 (0.32, 0.78)
Lebanon	0.92 (0.58, 1.44)	4.22 (3.14, 6.14)	0.66 (0.36, 1.04)	0.74 (0.42, 1.16)
Libya	0.20 (0.00, 0.42)	-0.24 (-0.38, -0.06)	0.18 (0.02, 0.36)	0.20 (0.02, 0.40)

Morocco	0.34 (0.16, 0.54)	1.16 (0.54, 1.84)	0.28 (0.12, 0.46)	0.30 (0.14, 0.48)
Saudi Arabia	0.08 (-0.02, 0.40)	0.12 (-0.08, 0.46)	0.08 (-0.02, 0.34)	0.08 (-0.02, 0.38)
Syria	0.38 (0.18, 0.66)	0.82 (0.20, 1.70)	0.32 (0.14, 0.54)	0.34 (0.16, 0.56)
Tunisia	0.26 (0.12, 0.50)	1.56 (1.20, 2.08)	0.16 (0.04, 0.34)	0.18 (0.06, 0.40)
Turkey	0.22 (0.12, 0.42)	1.26 (0.92, 2.32)	0.10 (0.04, 0.30)	0.12 (0.04, 0.34)

*PWID: people who inject drugs

Table 3: The univariable and multivariable linear regression coefficients, with 95% confidence intervals (CI), showing the associations between demographic and epidemiological variables and (a) the number of infections averted per randomly allocated treatment, and (b) the number of infections averted per treatment allocated to PWID.

		Infections averted per randomly allocated treatment			
Variable	**Mean (Range) across country-level variable**	**Univariable regression coefficient (95% CI)**	**P-value**	**Multivariable regression coefficient (95% CI)**	**P-value**
Population growth rate (% increase in population per year)*	0.6% (-0.8%, 3.8%)	0.13 (0.10, 0.17)	<0.001	0.13 (0.08, 0.17)	<0.001
General Population chronic HCV prevalence (%)*	1.1% (0.1%, 6.0%)	-0.03 (-0.08, 0.03)	0.332	-0.07 (-0.12, -0.02)	0.008
PWID chronic HCV prevalence (%)*	37.2% (3.9%, 72.7%)	-0.009 (-0.012, -0.006)	<0.001	-0.007 (-0.010, -0.004)	<0.001
Population proportion of PWID (% of adults that are PWID)*	0.44% (0.02%, 3.95%)	-0.00 (-0.10, 0.10)	0.998	0.12 (0.02, 0.21)	0.017
Population Attributable Fraction of HCV due to IDU*	68.9% (1.6%, 100.0%)	-0.003 (-0.004, -0.001)	0.001	-0.001 (-0.003, 0.001)	0.465
Injecting duration (years)**	13.1 (4.4, 24.8)	-0.01 (-0.02, 0.00)	0.196	0.01 (-0.00, 0.02)	0.097
		Infections averted per PWID allocated treatment			
Population growth rate (% increase in population per year)*	0.6% (-0.8%, 3.8%)	0.46 (0.29, 0.63)	<0.001	0.20 (0.07, 0.33)	0.004
General Population chronic HCV prevalence (%)*	1.1% (0.1%, 6.0%)	-0.07 (-0.28, 0.14)	0.499	-0.25 (-0.40, -0.10)	0.002
PWID antibody HCV prevalence (%)*	37.2% (3.9%, 72.7%)	-0.058 (-0.067, -0.049)	<0.001	-0.047 (-0.056, -0.039)	<0.001
Population proportion of PWID (% of adults that are PWID)*	0.44% (0.02%, 3.95%)	-0.14 (-0.53, 0.25)	0.471	0.34 (0.06, 0.63)	0.019
Population Attributable Fraction of HCV due to IDU*	68.9% (1.6%, 100.0%)	-0.014 (-0.020, -0.008)	<0.001	-0.005 (-0.011, 0.000)	0.060
Injecting duration (years)**	13.1 (4.4, 24.8)	-0.08 (-0.12, -0.04)	<0.001	-0.02 (-0.05, 0.00)	0.063

*Per percentage point increase; **per year of injecting duration

HCV: Hepatitis C virus; PWID: People who inject drugs; IDU: Injecting drug use

Fig 1: Chronic HCV infections averted per HCV treatment over 20 years globally, and by region stratified by allocation strategy. Whiskers are 95% credibility intervals.

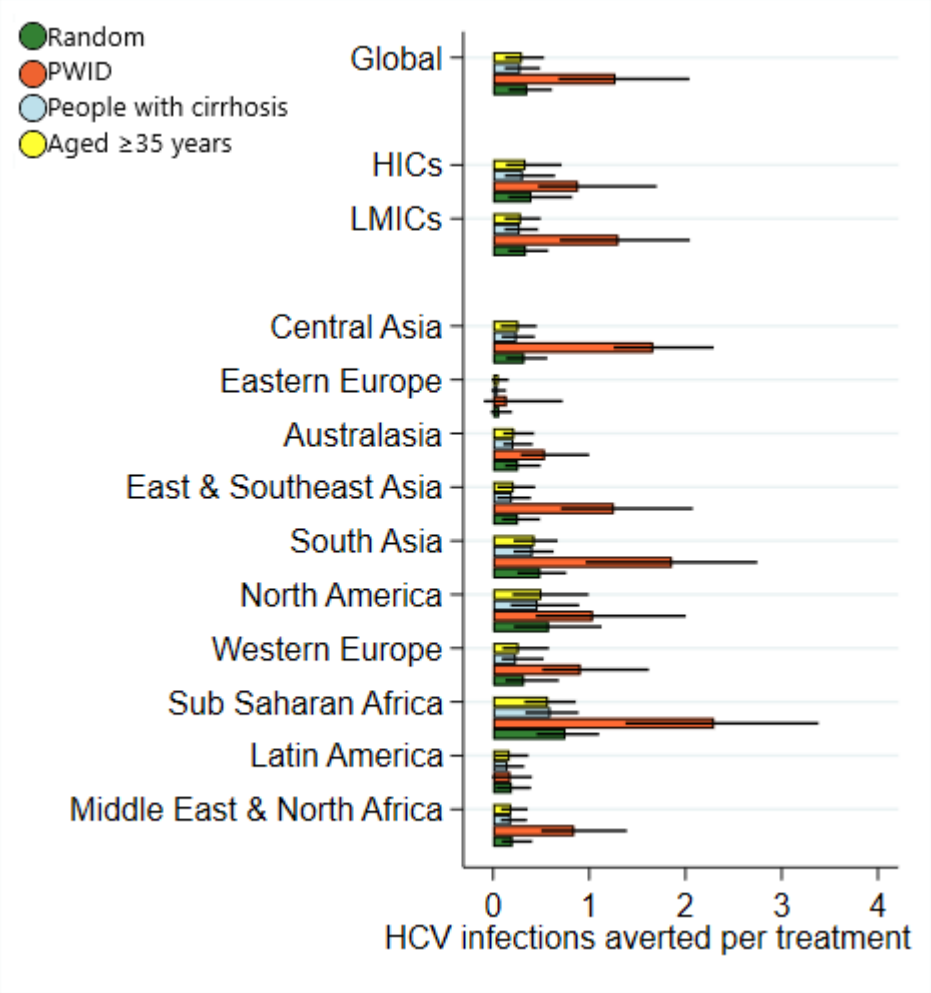
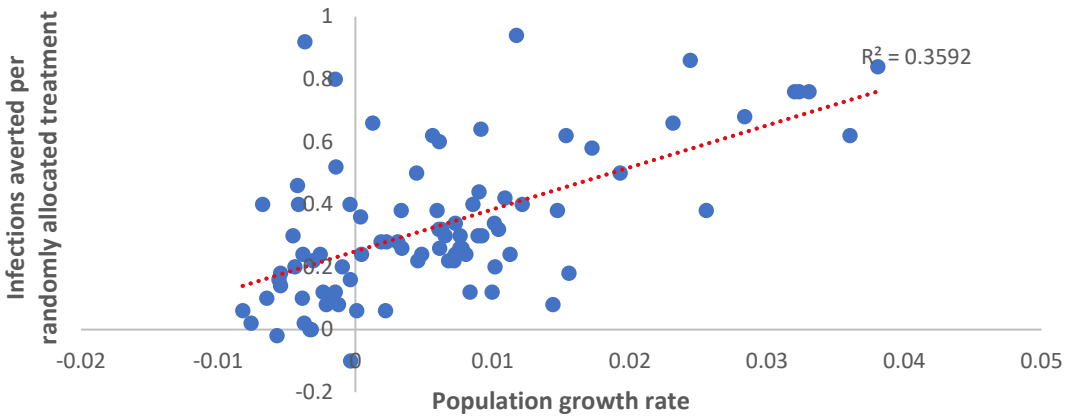


Fig 2: Scatter plots of the univariable associations between the number of HCV infections averted (over 20 years) per treatment given randomly, and a country's population growth rate (2a), or the antibody HCV prevalence among people who inject drugs (PWID) in 2015 (2b)

a)



b)

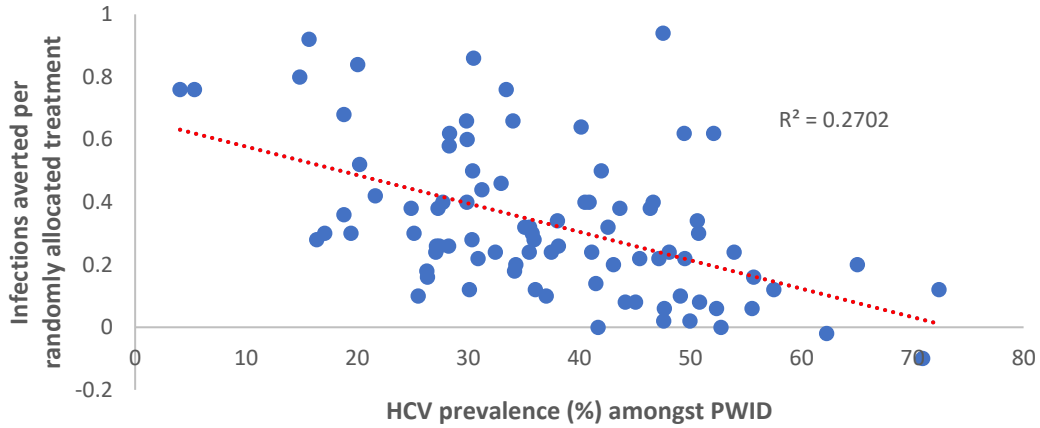
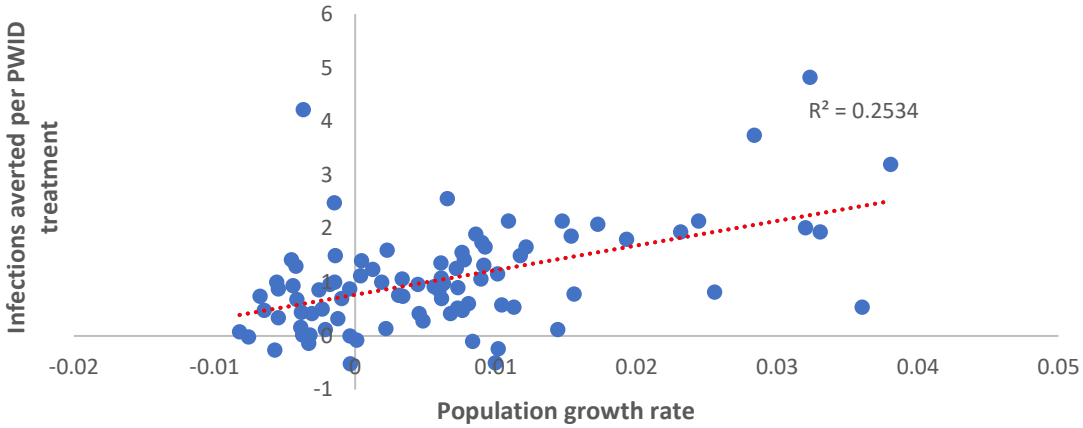
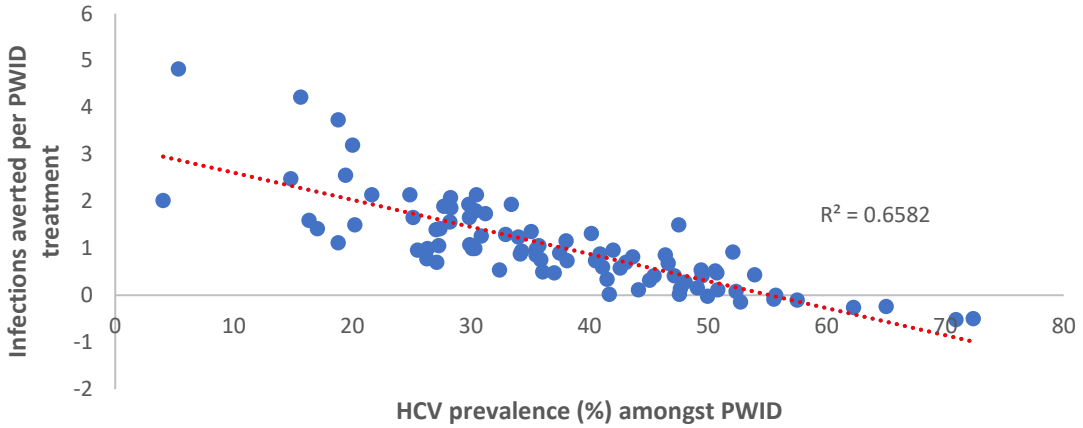


Fig 3: Scatter plots of the univariable associations between the number of HCV infections averted (over 20 years) per treatment given to people who inject drugs (PWID), and either a country's population growth rate (3a), or the antibody HCV prevalence among people who inject drugs (PWID) in 2015 (3b)

a)



b)



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